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# Perspectives in Venereology—1958

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This is the 12th of a series of annual reviews of the world's literature [this *Bulletin*, 1948, v. 23, 135–44; 1949, v. 24, 99–111; 1950, v. 25, 331–43; 1951, v. 26, 101–21; 1952, v. 27, 297–314; 1953, v. 28, 489–503; 1954, v. 29, 541–62; 1955, v. 30, 453–73; 1956, v. 31, 769–87; 1957, v. 32, 521–43 and 1958, v. 33, 901–22].

## Introduction

The most significant development of the year has been the rising attack rate of gonorrhoea, particularly in England and Wales but also in a number of other countries. In some of the larger British clinics the case load of new male cases of gonorrhoea has more than doubled during the last 3–4 years. This has arisen from a number of medical and social reasons but at the same time has been associated with a definite deterioration in the results of treatment of gonorrhoea with repository penicillins. A declining sensitivity of the gonococcus to penicillin (and streptomycin also where it has enjoyed wide usage for a long period of time) is becoming increasingly apparent in a number of countries.

This situation is disturbing and is dictating a shift from repository penicillin preparations to larger doses of quicker-acting non-repository preparations capable of producing a higher serum barrier of penicillin which is less likely to foster further resistance of the gonococcus. The use of other antibiotics and combinations of antibiotics are all under consideration but the general consensus of opinion is that penicillin is still a good drug in the treatment of gonorrhoea and should continue to be exploited to the fullest advantage as long as it remains so. As, with whatever antibiotics are used, some failures still occur it is felt likely that the problem of a declining sensitivity of the gonococcus to antibiotics plus a rising or sustained attack rate is likely to continue.

Syphilis, happily, continues to decline or remain more or less static at a very low level. It is felt that the use of repository penicillins for gonorrhoea—with the prolonged penicillinaemia they provided—has contributed materially to the reduction of syphilis by cutting it off in the incubation period. It remains to be seen whether the use of shorter-acting preparations in gonorrhoea results in a higher attack rate of syphilis.

The increasing problem of allergic reactions to penicillin, especially serious and even fatal anaphylactic reactions, is also a matter of concern. Although still uncommon in relation to the enormous amount of penicillin used they are increasing in frequency as more and more patients become "penicillinized". They are more commonly encountered in the treatment of syphilis for which many injections are used than in gonorrhoea where only one is usually given. As syphilis becomes rarer and increasing numbers of patients attend with repeated gonococcal infections these reactions are becoming almost as great a problem in this disease also. While the discouragement of the indiscriminate use of antibiotics will help to reduce the development of both resistance and allergic reactions, the seriousness of the latter can be minimized by having an emergency kit in the clinic so that adrenaline hydrochloride and other life-saving drugs can promptly be given. The anti-penicillin enzyme penicillinase holds promise in the treatment of penicillin reactions.

In the laboratory simpler specific serum tests for syphilis involving treponemal antigens, which give results comparable with those of the more expensive and cumbersome treponemal immobilization test, have been evolved. Their performance is within the powers of the average serological laboratory.

The cause of non-gonococcal urethritis remains undiscovered while the numbers of cases seen in the VD clinics of England and Wales have steadily risen each year since they were first published in 1951. In addition, the venereal aspects of trichomoniasis are being more forcibly stressed.

In summary the waters of venerology are far from settled. There is much to be done, and much of interest to be found, by young medical men taking up this speciality, whereas a few years ago they were discouraged from doing so by the mistaken but no longer so audible opinion that the venereal diseases as a public health problem had been conquered.

## Antibiotics

Penicillin reactions, which are commonly reported to occur in 1–5% of patients, were considered by the *Lancet* (1957, 1957a), by Dobson *et al.* (1957), by Schindel (1958), and in considerable detail in a series of 13 papers by the three authors Guthe, Idsøe and Willcox (1957, 1958) in various permutations.

Of the different reactions to antibiotics anaphylaxis is both the most dramatic and most serious and therefore attracts the greatest attention. Welch *et al.* (1957, 1958) in a survey of physicians in charge of 198,332 American hospital beds, noted 1,070 life-threatening reactions in the patients, of which over 80% were due to penicillin. The fatality rate from anaphylaxis was 9·1%, from severe dermal reactions 10%, and from angio-oedema of the respiratory tract 13% of those so affected. Idsøe and Wang (1958) reported 106 penicillin reactions from Taiwan in 1951–1955. There were 74 examples of anaphylaxis, 12 of which had proved fatal. Such events can understandably hamper a venereal disease control programme based on the use of penicillin. Even in New York, where 30 fatal cases have been reported, 9 are or have been subjects of law suits (Rosenthal, 1958).

Anaphylactic and other serious reactions are relatively very rare, however, in proportion to the enormous amounts of penicillin used. For example, Willcox (1958) reported on a WHO survey covering 626,551 patients over a 5-year period. There were only 9 deaths, mainly from anaphylaxis, or 1 in 69,600 cases treated. Of 12,858 naval recruits given benzathine penicillin McFarland (1958) reported a reaction rate of only 1·3% and in but one case in a 1,000 was it serious enough to require cortisone.

From Britain 12 cases of immediate reactions to penicillin were included in a study initiated by the College of Practitioners in London (Lewis, 1957). A case of severe anaphylactic reaction following the sucking of a penicillin lozenge (4 years after a similar episode) was reported by Gullatt (1957). Anaphylaxis can even occur in persons receiving daily steroids; Bernstein and Lustberg (1957) reported one such case in which the use of adrenaline was probably life-saving.

The best methods of preventing penicillin reactions are by taking a history of previous allergy, especially of penicillin sensitivity, before administering the antibiotic, and avoiding the use of it except on sound therapeutic and prophylactic indications. Even so penicillin sensitivity *may* occur from food. Rosenthal (1958) reported that 5·9–11·6% of milk samples in New York City contained 2–80 units of penicillin per glass. Even cross sensitization with other fungi (*e.g.* from athlete's foot) has been considered. That the air and dust from, and the skin and nerves of workers in, hospital and penicillin factories carry appreciable amounts of penicillin was indicated by Gould (1958). The routine use of skin tests for predetermining patients likely to show allergic reactions to penicillin is not generally helpful. Even a skin test can cause severe reactions—as the case of stillbirth following an intradermal test reported by T'ao Jen and Sung Chieh (1958). Useful in minimizing the seriousness of such reactions is the keeping of an emergency pack, in clinics and consulting rooms where penicillin is given, which contains sterile syringes, adrenaline hydrochloride, intramuscular antihistamine and cortisone preparations, and intravenous aminophylline (*Lancet*, 1957; Willcox, 1958a).

An increasing number of reports concern the successful use of penicillinase in penicillin reactions (*Brit. Med. J.*, 1958); Willcox (1958b). Although there are few reports of the action of this penicillin-inactivating enzyme in anaphylaxis an intramuscular dose of 800,000 units (2 ml.) has been recommended in this condition (Zimmerman, 1958, 1958a). Steroids and antihistamines can also be used to suppress symptoms. Penicillinase may be useful in the differential diagnosis of a number of possible antigens. After its use there is no circulating penicillin within 15–60 minutes, reported Becker (1958, 1958a) who gave it with good results to 48 patients with mainly dermatological allergic reactions due to penicillin, in 24 instances without other drugs, Chen *et al.* (1958) likewise found the preparation to be lacking in toxicity and antigenicity.

Warren (1958) used Pabalate, a preparation containing 300 mgm. each of sodium salicylate and sodium *p*-aminobenzoate, with 50 mgm. of ascorbic acid, in 10 penicillin-sensitive patients with promising results.

Problems arising from the lessened sensitivity of the gonococcus to penicillin are discussed in the section on gonorrhoea below. Blood levels of penicillin, certainly insufficiently high to cure gonorrhoea, were obtained when 300,000 units of benzathine penicillin were given orally by GRIFFITH (1958). COLQUHOUN *et al.* (1957) noted that patients with pernicious anaemia had higher mean serum concentrations of penicillin than healthy patients when benzathine penicillin was given by this route. KRUGMAN and EBIN (1958) studied the local reactions which were noted in 54% of subjects given benzathine penicillin intramuscularly. If procaine penicillin was added to the suspension before use the local reaction rate was reduced to 11·5% and if prednisolone was used to 9·0%.

Of reactions to other antibiotics the effects of streptomycin on hearing were considered by CAWTHORNE and RANGER (1957) who reported 14 cases in which 1 gm. daily to a total of less than 20 gm. had caused toxic symptoms. Purpuric skin rashes and liver necrosis were reported following novobiocin by BRIDGES *et al.* (1957).

JONES and FINLAND (1957) failed to demonstrate synergism between tetracycline and oleandomycin, spiramycin and other agents. ELLIOTT and HALL (1957) also studied the action of combined antibiotics against staphylococci: effects were usually additive.

## Chancroid

A comparison of antigens produced in Japan and the United States for skin tests in the diagnosis of chancroid was made by BOAK (1957).

## Gonorrhoea

### *General*

Gonorrhoea in the female was considered by PARKER (1958). DUREL (1957), writing from France, noted that although many countries reported a 50–70% drop in the clinic incidence of gonorrhoea during the years 1946–1950 there had been little change during the past 5 years. Much work was required for the detection and treatment of gonorrhoea in female contacts and the prevention of reinfection. In France, he calculated, 60% of prostitutes were infected. In England and Wales in 1956 there was a sharp rise in both sexes to 20,388 cases from 17,845 the previous year (17,536 in 1954 and 18,064 in 1951) according to Ministry of Health figures (*Brit. J. Venereal Dis.*, 1958).

Much gonorrhoea occurs in promiscuous persons who have previously had the disease. WATT (1958), reporting from Manchester, noted that of 1,482 males with gonorrhoea seen in 1955–56 only 810 (54·6%) had first infections. The remaining 672 (45·4%) had had no less than 1,261 previous attacks. More than half of the new infections occurred in immigrants.

### *Pathology*

The properties of the gonococcus endotoxin were considered by TAUBER and GARSON (1957). The same authors (1958) noted that cortisone protected mice from the endotoxin and that, provided sufficiently large doses were used, properdin would do likewise. Reserpine, on the other hand, under certain conditions significantly enhanced the toxicity of endotoxin. (Bacteriological problems concerned with developing resistance to gonococci to antibiotics are considered under *Treatment*.)

### *Treatment*

The treatment of gonorrhoea in the male was considered by STEPPERT (1958) and by SHAH (1958). Phenoxymethyl penicillin (penicillin V) was given to 76 patients by RAJAM *et al.* (1958), intensively for 1 day then once daily for 8–14 days, with cures in 97·4%. WILLCOX (1958c) treated 85 male patients with 1–2 oral doses of 2–3 mega units of penicillin V. In 33 white patients there were 14·8% of recurrences (all suspected of being reinfections). In 52 coloured patients there were 40·8% of recurrences, 7 of 10 of which were considered to be failures.

With penicillin by injection there have been increasing failure rates through the years in spite of increasing dosage. An increase from 0·25 to 4·4% of failures was reported in females in Vienna by STREITMANN and KRASSNIGG (1957). In London, WILLCOX (1958d) reported a failure rate as high as 17·9% with single doses of as much as 1·2 mega units of procaine penicillin with aluminium monostearate, and no less than 30·4% with the same dose of benzathine penicillin.

In some areas it has been the practice to give large doses (*e.g.* 2·4 mega units) of benzathine penicillin to the female contacts of male patients with gonorrhoea, irrespective of whether or not they have been proved to be infected, in order to cut down the rate of reinfection. Such was considered by TAKOS *et al.* (1957) to have contributed to a steady fall in incidence in Dave County, Florida. SCHAMBERG *et al.* (1958) used this so-called antibiotic quarantine in both sexes, giving 2·4 mega units of benzathine penicillin to 2,400 male and to 1,700 female patients. The females were asked to return every 8 weeks for the same treatment. The success rate was high but gonococci were recovered within 8 weeks in 0·5% of females and in 0·25% of men. That the gonococcus can surmount the penicillinaemia provided by even large doses of benzathine penicillin (and that its use might further foster the breeding of less sensitive strains of gonococci) was indicated by one case in which gonococci persisted for 6 months in spite of repeated doses of benzathine penicillin up to 4·8 mega units. The authors concluded that 2·4 mega units of benzathine penicillin gave a penicillinaemia for 50 or more days sufficient to kill 95% of strains, but not the most resistant strains. The quicker-acting procaine penicillin capable of producing a higher peak level (0·6 mega units) is currently being used with 1·2 mega units of benzathine penicillin to prevent dissemination.

CRADOCK-WATSON *et al.* (1958), in the laboratory, noted that whereas 162 strains of gonococci were inhibited by 0·064 unit of penicillin per ml., 16 required 0·256 unit/ml. and 5 strains needed 0·512 unit/ml. They too concluded that 0·6 mega units of procaine penicillin should be used in place of longer-acting repository preparations, but by itself.

In another series of 302 strains of gonococci tested by **Curtis** and **Wilkinson** (1958) in 19·5% the sensitivity to penicillin ranged between 0·125 and 0·5 unit per ml. and the failures of treatment with this antibiotic were found to occur mainly in patients whose gonococci initially showed these relatively low sensitivities. These workers stressed the need for a penicillin preparation capable of providing a penicillinaemia of at least 1 unit/ml. for 24 hours and, for the present, also recommended procaine penicillin in a dosage of 0·6–1·2 mega units. **Landman** *et al.* (1958), who previously had used 1·2 mega units of benzathine penicillin in the female, likewise urged the provision of a higher peak serum level by the use of fortified preparations.

**Dallas** (1958) made an assessment of 63 so-called penicillin failures in 447 cases. He found that in only 4·4% was the recurrence noted within 2 weeks of treatment and believed that the reappearance of the gonococcus after 2–3 weeks indicated a reinfection irrespective of the history obtained.

**Reyn** *et al.* (1958) contrasted 296 strains of gonococci isolated in Copenhagen during the years 1944 and 1957. A lowered sensitivity was noted to penicillin in the 1957 strains but this was not striking in respect of streptomycin or tetracycline. These workers also considered a new penicillin schedule to be necessary.

Both **Willcox** (1958e) and **Knight** (1958) have reported higher failure rates in Negroes than in white-skinned persons, indicating a possible quicker development of resistance in this group and their mainly prostitute consorts resulting from repeated treatments with penicillin for reinfections with gonorrhoea.

Should the gonococcus become markedly resistant to penicillin there are of course other antibiotics—streptomycin, the tetracyclines, chloramphenicol, erythromycin, spiramycin and oleandomycin, all of which can cure the disease. With all of them, however, there is usually a substantial relapse rate (about 10%) in the dosages so far used (**Willcox**, 1958d). Novobiocin is not effective unless given in the relatively high dosage of 8–10 gm. when a success rate of 66–78% may be achieved (**Willcox**, 1957).

Very promising results (100% success) were reported from the U.S.A. with 1·5 gm. of tetracycline hydrochloride given orally and with only 1 gm. of the newer tetracycline phosphate complex by **Schultz** and **Shaffer** (1958). The problems of high recurrence rates, however, are not so commonly reported in the American literature as in the British, and the same authors reported 97·0% success with 600,000 units of procaine penicillin with aluminium monostearate given by injection.

The increasing failure rates to treatment are not confined to penicillin. **Alergant** (1958) reported from Liverpool that in three series (each of over 200 cases) in which 0·5 gm. of streptomycin was used the failure rate in 1954 was 2·3%, but by 1956 had reached 7·0%. He claimed that resistance was developing. The problem of resistance of the gonococcus to streptomycin is even more acute in France where for many years this antibiotic has been used routinely for gonorrhoea in preference to penicillin. Apart from changing antibiotics another method to combat resistance is to use combined antibiotics, for instance penicillin and streptomycin as given by **Mikhailov** (1957).

For the present it would seem wise to adhere to the use of penicillin, keeping the other antibiotics in reserve with their edges unblunted by widespread usage. But the penicillin preparation employed should be shorter-acting, capable of producing a serum level with a high peak of relatively short duration, thus providing a higher hurdle over which the gonococcus is unlikely to pass for some time, and cutting off quickly so that persons re-exposing themselves do not offer fresh strains of gonococci low surmountable levels to overcome. Of the preparations available procaine penicillin in a single injection of 1·2–1·5 mega units would appear to be the best. In any event the situation is most disquieting. With the increasingly high attack rate (as shown in Birmingham by **Knight** (1958) where the numbers of new male cases were 444 in 1955 and 1,063 in 1957) and increasing failure rates to treatment—with little hope of being able to do much more to prevent this trend than to try to slow it down—there is no room for complacency.

### *Complications*

A case of gonococcal bulbitis was described by **Rousset** *et al.* (1958). Local injections of hydrocortisone (3 or less) after dilatation were stated to be successful in the treatment of 51 of 56 urethral strictures by **Lyons** and **Bonner** (1957). The principal complication in the female is salpingitis. **Landman** *et al.* (1958) described 1,604 patients with salpingitis (gonococcus-positive in 41·5%).

Venereal diseases in the new-born, including gonococcal ophthalmia, were described by **Willcox** (1957a), and the surprising relative rarity of gonococcal ophthalmia in Africa was noted by **Rodger** (1958).

That the use of silver nitrate prophylactic drops would not entirely abolish gonococcal ophthalmia was indicated by **Pearson** (1957) who observed 40 cases in 67,200 live births during 10 years in which silver nitrate was given routinely. The ease with which gonococcal ophthalmia may be treated has led, in areas where post-natal supervision is satisfactory, to a relaxation of prophylactic measures against this complaint; thus obviating the risk of chemical conjunctivitis from the drops themselves. For example, in New York City, the Board of Health has repealed the Sanitary Code, and specific prophylaxis against gonococcal ophthalmia is no longer obligatory; private physicians can continue the practice if they wish. An editorial in *Internat. Med. Digest* (1958) expressed the hope that the practice would not be widely adopted. **Hertzberg** (1957), in Australia, considered that with adequate hospital facilities the swabbing of the eyes before they were opened was all that was necessary but silver nitrate should be used if the surroundings or antenatal care were unsatisfactory (see also *Med. J. Australia*, 1957).

Much depends on what constitutes a local reaction. Silver nitrate and oxytetracycline were compared by **Mathieu** (1958). No less than 46% of infants developed some ocular discharge with silver nitrate compared with only 6% when 0·5% oxytetracycline was used. On the other hand, local reactions were noted in only 41 of 1,205 infants given silver nitrate by HARRIS (1957) as compared with 33 of 1,219 infants in whom penicillin was applied. MARGILETH (1957) reported 50% of local reactions with silver nitrate. Of 5,394 babies given penicillin drops (5,000 units per ml.) 59 had mild or moderate reactions and 3·2 per cent. developed an eye infection. With bacitracin ointment (500 units per gm.) 21 of 2,380 babies had mild or moderate reactions and 1·6% developed an eye infection. Routine therapy was not advised: cases should be treated as they arise. Bacitracin ointment (500 units per gm.) plus 2% phenacaine hydrochloride also proved satisfactory in 1,144 babies treated by ANDERSON and POSNER (1958). BREUNING (1957) recommended an oily solution of penicillin claiming only 1 failure and no side-effects in 15,000 cases treated. SCHILLING (1958) found 30% sulphacetamide or 30% Albucid satisfactory in 9,000 infants. Desogen, a quaternary ammonium compound, has been used in ophthalmia prophylaxis by SALVISBERG and SCHONENBERGER (1957) and by RINTELEN and HOTZ (1957).

## Granuloma Inguinale

Of 61 patients with donovanosis reported by MARMELL (1958) 51 had genital or inguinal lesions and 10 had anal lesions. Of these 9 admitted to homosexual practices. Granuloma inguinale in a Jamaican and his wife in London was reported by BARROW (1958); it is rare for conjugal cases to be found. A case of granuloma inguinale in the epididymis in a Caucasian male, confirmed after operation in Japan, was recorded by JANNACH (1958). The man complained of pain and the affected epididymis was nodular and shrunken. A case of metastatic granuloma inguinale in bone was reported by RAJAM *et al.* (1957a).

## Lymphogranuloma Venereum

6 cases of lymphogranuloma venereum in the United Kingdom were reported by GALBRAITH *et al.* (1957) who considered a future increase not unlikely as a result of West Indian immigration. Rectal lymphogranuloma venereum was described by MILES (1957), and the opinion that lymphogranuloma venereum might simulate ulcerative colitis was stated by GOLDGRABER and KIRSNER (1957), and that cancer might coexist with lymphogranuloma venereum by WRIGHT (1958).

HILLEMAN *et al.* (1958) reported on the use of the viruses of psittacosis, ornithosis, lymphogranuloma venereum, and feline and mouse pneumonitis in skin testing for lymphogranuloma venereum. All were found to be satisfactory, but those of mouse or feline pneumonitis were recommended for use as the best skin test antigens as they are non-pathogenic for man.

ERSKINE (1958) reviewed 61 cases of lymphogranuloma venereum seen over the years in London. Oxytetracycline in one or two 10-day courses of 20 gm. each was considered to be the drug of choice. Clinical cure was noted in all of 26 patients followed out of 32 treated.

## Non-Gonococcal Urethritis

### *Epidemiology*

Non-gonococcal inflammatory diseases of the urethra were considered by PORUDOMINSKI (1957).

A symposium on non-gonococcal urethritis was held at Catania during 1957 (*Minerva Dermatologica*, 1957). The disease continues to be prevalent in many parts of the world. The figure of 16,066 cases for the United Kingdom in 1957 was the highest since the figures were first published in 1951. MARSHALL (1957) reported that during a 7-month period, in 1956, of a ship's complement of 900 men there were 310 cases of VD, of which 152 were non-gonococcal urethritis.

The epidemiology of non-gonococcal urethritis was considered by BOYD *et al.* (1958) who contrasted 200 cases of this condition with 200 of gonorrhoea. In non-gonococcal urethritis the relationship with extramarital intercourse was less definite (22% denied recent sexual exposure) and the time-interval between exposure and symptoms presented no definite pattern. Masturbation was practised regularly by 51 of the patients with non-gonococcal urethritis as compared with only 27 of those with gonorrhoea, although this difference was largely confined to one of the two clinics contributing to the study. No relationship between non-gonococcal urethritis and the previous injection of antibiotics was noted. The medico-social pattern of non-gonococcal urethritis was also studied by MACFARLANE and JOHNS (1958). The group with non-gonococcal urethritis contained more older and more married men than the gonorrhoea group, members of which were probably more promiscuous. Of 250 men with non-gonococcal urethritis no female contact was named twice, whereas this event occurred 6 times in 100 male cases of gonorrhoea.

### *Pathology*

Urethral washings from 24 patients with non-gonococcal urethritis (and also the synovial exudate from 2 with Reiter's syndrome) were investigated in Chang conjunctival and amnion cell cultures for the production of viral cytopathogenic effects by FORD (1958) but nothing significant was found. The growth of pleuropneumonia-like organisms, whose claim to be responsible for non-gonococcal urethritis is less strong than formerly, was studied in human epidermoid carcinoma cells (HeLa) by SHEPARD (1958). Pleuropneumonia-like organisms were, however, considered by BERG *et al.* (1957) to be responsible for acute haemorrhagic cystitis. They proved sensitive to streptomycin and tetracycline but not to penicillin or sulphonamides.

Trichomonas urethritis in the male, believed by McDONALD (1958) to be probably venereal, was considered by NICOL (1958). Of 583 patients with non-gonococcal urethritis *T. vaginalis* was found by microscopy in 32 (5·5%). The percentage was increased to 8·6 if cultures were used, and the parasite was more commonly encountered in coloured than in white patients. DUREL (1957a) stated that trichomonads were variously reported as present in 9–41% of cases.

Difficulties in diagnosing prostatitis have been emphasized. GARTMAN (1958) made a comprehensive study of this condition and found over 15 leucocytes per high power field in the prostatic secretion in 54·1–68·5% of 3 groups comprising 264 young men. OATES (1958) accepted 10 or more cells in the expressed secretion as indicative of prostatitis (clumping nearly always being present) but recommended that a 5-slide test be made.

### *Clinical*

A case of non-gonococcal urethritis due to *Candida albicans*, in which cheesy excrescences were seen through the urethroscope, was reported in a diabetic by FOWLER (1958).

The Fiessinger-Leroy-Reiter syndrome was studied by MAVIOGLU (1958) on the basis of 132 cases in the literature (87 references). The recurrence rate was 38·5% of patients. The course of Reiter's syndrome was considered in detail on 185 patients by CSONKA (1958) while MORTON (1958) reported examples in first cousins. The condition is rarely found in females but 3 cases were reported by REFVEM (1958) in which polyarthritis and a raised blood sedimentation rate were noted. Two patients had conjunctivitis but only one had urethritis, and it was considered that in the female vulvo-vaginitis should be accepted as the genital moiety of the triad.

Prostatitis was found in 95% of 59 cases of Reiter's disease by MASON *et al.* (1958), while of 74 patients with uveitis seen by CATTERALL (1958) 17 had Reiter's disease. The radiographic appearances of Reiter's disease were studied by MURRAY *et al.* (1958) on 53 patients, and on 58 male and 2 female patients of a larger series of 185 cases by REYNOLDS and CSONKA (1958). The latter reported that the distal joints of the lower extremity were those most commonly affected, the knees and ankles in over 70%, and the hands and wrists in over 55%. The sacro-iliac joints were involved in 9% and there was bony ankylosis, mainly of the small joints of the feet, in 8 cases. Sacro-iliitis in Reiter's disease was considered, with radiographic illustrations, by OATES (1958a).

### *Treatment*

In the treatment of uncomplicated non-gonococcal urethritis the tetracycline antibiotics continue to give the best results. WILLCOX (1958f) reported only 18·5% of failures in 124 cases in which 6 gm. of tetracycline was given over 6 days. The same author (1958g) used spiramycin on 123 patients and had 25 failures (20·3%), and gave tetracycline and oleandomycin (Sigmamycin) to 62 patients (WILLCOX 1958h); in the last-named series there were only 7 failures in 51 patients followed. OATES (1958b) likewise used the tetracycline and oleandomycin combination on 33 patients with 5 relapses and 1 failure (trichomonas-positive) and believed the combined preparation to be very effective.

The necessity for giving expensive antibiotics for a condition which is largely self-limiting has been questioned. HANDFORTH (1958) considered that antibiotics should be reserved for severe cases only. Of 275 service patients only 20% were given antibiotics and the remaining 80% were not treated. FOWLER (1958a), in a study of 242 cases of non-gonococcal urethritis treated only with a citrate mixture, found that 78·7% showed spontaneous recovery within 5 weeks. He considered sulphonamides and streptomycin to be ineffective, and oxytetracycline, allowing for spontaneous recovery, to be of ultimate practical value only in some 14% of cases.

In chronic cases local treatment may be necessary. Urethral suppositories of Furacin were used for 2–3 weeks by WILLCOX (1958i) in 23 patients; there were 4 failures and 5 relapses. Although no strong curative claims were advanced, this was regarded as a useful ancillary treatment when irrigations were difficult to arrange. Local measures are usually required for trichomonas urethritis. ANGEL GARZA (1958) found that mapharsen (0·06 gm. in ½ litre of water) was a satisfactory solution in 24 cases. DUREL (1957a), in listing treatments used, included conessine (Roquessine), an alkaloid extracted from various species of *Holarrhena* and applied locally.

## **Other Conditions**

Two cases of chronic benign circumscribed plasma-cell balano-posthitis with characteristic histology were recorded by FOWLER (1958b).

The year has shown an added emphasis of the importance of chronic prostatic infection as a cause of ocular and rheumatic complaints. MASON *et al.* (1958) found evidence of prostatitis in 83% of 54 males with ankylosing spondylitis, 95% of 59 with Reiter's disease and in 33% of 86 with rheumatoid arthritis. CATTERALL (1958) investigated 74 patients with uveitis and found chronic prostatitis in 58 (74·4%). 8 of the patients had ankylosing spondylitis, 17 had Reiter's disease and 2 had plantar fasciitis. Pleuropneumonia-like organisms (PPLO) were grown from the urine or prostatic fluid in only 7 of 70 patients studied and a complement-fixation test with PPLO as an antigen was positive in only 14 of 70 specimens tested (20%).

### *Trichomoniasis*

The proceedings of the First European Symposium on Trichomonal Infections, held at Rheims in 1957, have been published (*Soc. Française Gynecol.*, 1957). *T. vaginalis* infections in the male are considered under " non-gonococcal urethritis ". That *T. vaginalis* infection is definitely a venereal infection in the male but perhaps not always in the female was the opinion of DUREL and ROIRON (1957). HODGSON (1958), on the other hand, considered that the condition was probably not infectious and not venereal, and that too much ado was being made of a minor disorder mainly of women which was associated with the wearing of tight clothing over the perineum.

The culture of trichomonads was considered by FEINBERG and WHITTINGTON (1957), *Brit. Med. J.* (1958a), FEO (1958) and by WILKINSON and WILLIAMS (1958). WELD and KEAN (1958) studied *T. vaginalis* in the eye of the rabbit. If the anterior chamber was inoculated with the parasite no trichomonads could be found after 2 hours but infection of the eye did occur if the lens was injured. The parasite grew well in the vitreous body but did not spread to other tissues.

McEntegart *et al.* (1958) described preliminary experiments with fluorescent antisera in the detection of serological varieties of *T. vaginalis.* Fluorescent techniques certainly distinguished between *T. vaginalis* and *T. foetus.* Agglutination tests were made by Lanceley (1958). Immune sera prepared against *T. vaginalis* showed agglutinating antibodies. 20 specimens of *T. vaginalis* were tested against this immune serum: 18 were agglutinated and 2 were not agglutinated. 4 immune sera were prepared from different specimens of *T. vaginalis.* Cross agglutination tests indicated that 2 of the sera contained different agglutinins.

The diagnosis and treatment of vaginitis were considered by Lammert (1958). Lamy (1957) believed that differences in the activity of various antibiotics in trichomonas vaginitis probably depended on the antibiotic sensitivity of the other vaginal flora.

2-acetylamino-5-nitrothiazole (aminitrozole) was given orally in a dose of 100 mgm. 3 times a day for 10 days to 8 patients by Dunlop *et al.* (1958). Trichomonads were, however, still found in 36 of 39 post-treatment observations. Feo and Fetter (1958) found that a dosage of 100 mgm. given 3–4 times a day for periods up to 10 days was not effective, but doses of 300 mgm. 4 times a day had therapeutic potentialities though the toxic effects then experienced were too great to justify general use.

Various pessaries continue to be recommended. Baum (1958) recommended silver picrate suppositories and Weiner (1958) preferred Vagisec liquid and jelly. Karnaky (1958) found useful a complex powder which kept the vagina at a *p*H of 2·0–2·5. Locan pessaries containing amethocaine and amylocaine were recommended by Stewart *et al.* (1957) who reported that 84% of infections were controlled after one week. Raddin (1957), using a regime based on Floraquin, claimed only 1 relapse in 20 years of experience. He considered that if trichomonas vaginitis *was* a venereal disease there would be more reinfections from the husband. [In fact, clinicians are constantly worried by recurrences, and reinfection from the consort is considered as probably responsible for a number of these.]

## Syphilis

### *History*

Syphilis in the Shakespearian tragedies was considered by Hahn (1958); *Timon of Athens* was not considered a lesser play but a classic source of information in this connexion. A new revision has been made of the excellent U.S. film *The Invader* which describes the history of syphilis. The new version runs for 29 minutes (*Soc. Hyg. News*, 1958).

That syphilis had been introduced into Canton by the end of the 13th century, into the Yangtze area during the 15th century, and thence over the entire country of China, was the conclusion of Lee T'ao (1958); local names for the disease include " Canton ulcers " and " strawberry sores ".

### *General*

A further annual review of the literature concerning syphilis has been made by Beerman *et al.* (1958).

De Graciansky and Grupper (1957) studied the effects of cortisone and penicillin in syphilis and concluded that under cortisone the Herxheimer reaction (clinical and febrile) was attenuated at all stages of the disease but claimed that, although the clinical manifestations were ameliorated, the condition was not cured by cortisone alone. Cortisone and immunity in syphilis were studied by Lesinski *et al.* (1958).

Hill *et al.* (1957) considered the long-term effects of syphilis in the Bantu and European. Signs of the disease were found at post mortem in 5·5% of Bantu subjects but in only 0·5% of Europeans. Assuming that only half of the patients showed signs of the disease infection was assumed in 11% and 1%, respectively. The surgical aspects of syphilis in the tropics were considered by Carayon *et al.* (1958).

### *Experimental Syphilis*

Longhin *et al.* (1957) kept syphilitic rabbits at various temperatures. Those kept at 20°C. and at 11–15°C. showed no signs of generalization of the disease but 42·8% of those kept at the lower temperature of −6°C. did so. Pautrizel *et al.* (1957) queried why no congenital syphilis was found in rabbits. Syphilitic foetuses were not found in pregnant infected rabbits and neither would the disease develop if the foetus was inoculated *in utero* with *Trep. pallidum.* They showed that neither rabbit amniotic fluid, extract of foetal tissues, nor blood from the foetus itself could immobilize or destroy spirochaetes.

Musumeci *et al.* (1958) studied the effect of penicillin on the behaviour of bismuth in rabbits after treatment with the salicylate labelled with radioactive bismuth. Wicher and Rogala (1957) found the Donath-Landsteiner reaction negative during the first year of infection in 68 syphilitic rabbits. Mutermilch and Gérard (1957) successfully treated syphilitic rabbits with spiramycin.

Heymann and Ihm (1957) studied the powers of neosalvarsan and penicillin to clear *Trep. pallidum* from the brains of mice. They found 20 mgm. of neosalvarsan sufficient to clear 93·7% of brains and 6,000 units of penicillin to do so in 100% of animals.

Berlinghoff (1957) studied the treponemal immobilization test in mouse syphilis. No positive TPI test was found, although rabbits inoculated from such mice developed a positive TPI reaction.

### *Trep. pallidum*

The activity of phosphonic and phosphinic acids on *Trep. pallidum* was considered by Doak *et al.* (1958), and Viaseleva (1957) studied the effects of penicillin on cultured *Trep. pallidum*, using the electron microscope (Viaseleva 1957a).

### *Early syphilis*

The masking of venereal diseases by antibiotics was considered by Zingsheim (1957).

A case of Follmann's primary syphilitic balanitis was reported by Tirlea *et al.* (1958), one of an irritating secondary syphilitic rash by Knight (1958a) and one of anetoderma following a nodular syphilide treated with penicillin by Duperrat *et al.* (1958).

The management of syphilis was reviewed by **Thomas** (1958) and epidemiological problems of early syphilis were considered by **Kolankowski** (1957) and by **Miedzinski** and **Markiewicz-Szumska** (1957). **Ullmo** (1958) reported the case of a husband and wife, each of whom not only had had two attacks of early syphilis but also each had been responsible for one of them. The tests of cure of syphilis were considered by **Langer** and **Kruger** (1957).

Penicillin in syphilis continues to give excellent results and the relatively low serum levels obtained with repository penicillins are quite sufficient to cure the disease provided a continuous penicillinaemia is maintained for a sufficient time. **Willcox** *et al.* (1958) reviewed 864 cases of primary and secondary syphilis treated at St. Mary's Hospital, London. Of 561 given penicillin plus a short course of arsenic and bismuth there were 7·2% of failures. Of 183 treated with penicillin and bismuth there were 9·2% of failures, but with penicillin alone (120 cases) the failure rate was only 3·6%. In this last series 4·8% mega units (in 8 daily injections of 600,000 units) of procaine penicillin with aluminium monostearate (PAM) were usually given, plus 10 twice weekly injections of 900,000 units.

The satisfactory use of "single-shot" treatments with 1·2 mega units of PAM were described by **Tuli** (1958) and short treatments generally by **Felke** (1958). **Rajam** *et al.* (1957a) treated 93 cases of primary and secondary syphilis with single injections of 2·4 mega units of benzathine penicillin (proportionately less for children) with satisfactory results although it was considered a disadvantage that many patients only attended once. **Montgomery** *et al.* (1958) treated 42 cases of early syphilis on a similar regime with only one failure, and that was considered to be due to reinfection. **Bolgert** and **Levy** (1957) treated 306 cases of early syphilis with 15 mega units of penicillin preceded by 3 injections of a mercury preparation given over 17 days. A success rate of 94·6% was claimed although, with the TPI test as a criterion, complete seronegativity might not be attained for some years.

The treatment of syphilis with antibiotics other than penicillin was reviewed by **Olansky** and **Garson** (1958). Chloramphenicol and the tetracyclines had been successfully used and carbomycin and erythromycin showed promise. **Wheeler** *et al.* (1957), stating that Synnetamin B had been noted to cure 2 cases of pinta in Mexico when being used in the treatment of typhoid fever, reported success in one case of primary syphilis. Novobiocin (cathomycin), on the other hand, in intravenous doses of 0·5 gm. given slowly twice daily for one week, failed in 3 cases of early syphilis in the hands of **Edelson** (1957).

### *Late benign syphilis*

The diagnosis, biology, and treatment of latent syphilis were considered by **Curtis** and **Schuster** (1958): 4·8 mega units of PAM were considered sufficient for cure. **Reboul** *et al.* (1958) again noted that the earlier the treatment was given the better the results. That the old-time arsenic and bismuth treatment was effective in latent syphilis in preventing the late complications was shown by **Kaplan** *et al.* (1958, 1958a); of 2,954 prisoners treated in Sing Sing prison between 1939 and 1949, who were subsequently observed for an average of 14 years, there was progress to neurosyphilis in only 0·3%. Seroreversal had occurred in 25% after 5 years and in 50% after 11 years.

Pathological findings in late syphilis in India were considered by **Sagher** and **Cohen** (1957). A fatal case of exceptionally severe gummatous osteitis of the skull, in which amyloid disease was found at post mortem, was reported by **Macfarlane** and **Rannie** (1958). A case of gummatous syphilis of the skin, 63 years after infection in a man of 81 years, was reported by **Masure** and **Brochen** (1958), another of gumma of the testicle was described by **Thiers** *et al.* (1958) and one of a tertiary syphilitic testicular abscess by **Rousset** *et al.* (1958a). A gumma of the spinal cord, occurring as precocious tertiarism in a male 16 years old only 5 months after an arsenical injection for primary syphilis, was described by **Rajam** *et al.* (1958a). 2 fatal cases of gumma of the lung were recorded by **Grandjean** (1958), syphilitic lesions of the main bronchi were considered by **Orlandi** (1957) and the differential diagnosis of gumma of the lung by **Timossi** *et al.* (1958).

Rheumatism and tertiary syphilis, including synovial, osseous and arthropathic lesions, was reviewed by **Losada** (1958), and a case of gummatous syphilis with rheumatic pains was recorded by **Ugazio** and **Barcia** (1956).

The use of potassium iodide as a diagnostic aid to increase positivity in late latent syphilis with weakly positive serum reactions, and as a therapeutic test for the treatment of possible gummata in patients in whom serum tests were not technically feasible, was recalled by **Hoffmann** (1957).

### *Cardiovascular syphilis*

**Raaschou-Nielsen** and **Kopp** (1957) studied 155 patients with neurosyphilis treated at Copenhagen in 1937–1952. Aortitis was found in 24, complicated in 8. Syphilitic aortitis was not considered to run a particularly mild course when it occurred in patients with neurosyphilis. The radiological signs of syphilitic aortitis were considered by **Lodwick** and **Gladstone** (1957) who described an "aortic index". Syphilis was present in 85% of those with an aortic index of 20 cm. or more and in 100% of those with an aortic index over 24·2 cm.

**Koulumies** and **Heinivaara** (1957) studied 112 patients with cardiovascular syphilis given 3·2–98 million units of procaine penicillin. Of 54 followed for 5 or more years only 23 were still living. Only 9% of those seen initially with uncompensated heart failure survived compared with 60·6% of those in whom the condition was compensated. Of 100 patients with syphilitic aortitis with involvement of the aortic valves seen by **Aceves** *et al.* (1957) there were 9 in whom bacterial endocarditis was superimposed.

Complicated syphilitic aortic aneurysms were considered by **Chand** *et al.* (1957). An unusually severe aneurysm was described by **Meyer** (1957) and a case of aneurysm of the ascending aorta in a 20-year-old congenital syphilitic by **Beard** and **Thompson** (1958).

The diagnosis of aortic aneurysm was reviewed by **Vernant** (1958). That reagin serum tests, and even sometimes the TPI test, may be negative in syphilitic aneurysm was noted by DI MATTEO (1958), although such tests would have been positive years previously. A case of syphilitic aortitis which could have been avoided had a premarital serum test been made was recorded by LAUGIER (1958).

A popliteal aneurysm which thrombosed 5 days after completion of a course of penicillin, and which occurred in a man aged 28, 6 years after receiving 4 unspecified injections for a bubo, was recorded by RAJAM and RANGIAH (1958). An improvement in a syphilitic aneurysm of the subclavian artery treated with chlortetracycline and cortisone was noted by THIERS *et al.* (1958a).

### *Neurosyphilis*

The significance of syphilis to the motorist and road safety was considered by PABST (1958). General paresis in French West Africa was reviewed by RAINAUT (1957, 1958) who considered it far more common than generally supposed. In Durban, South Africa, neurosyphilis was considered responsible for 0·5% of all hospital patients and 9·5% of neurological cases by WOODS (1957), who believed neurosyphilis to be a serious problem in the Bantu. HAHN *et al.* (1958) presented the findings of a cooperative study of 1,086 paretics attending 8 hospitals. The condition was 3 times as common in males as females, and twice as common in whites as in Negroes.

The psychosis of GPI was described by CLAMAN (1957), and the significance of minimal neurological changes in late syphilis by BARCIKOWSKA-STEMPIEN *et al.* (1957). A case of syphilitic thrombosis of the posterior inferior cerebellar artery was reported by RAJAM *et al.* (1958b). Hemianopia in a syphilitic subject was described by PLANQUES and COUADAU (1956) and the Argyll-Robertson pupil in diabetes by MOSCI (1957).

Problems in the clinical diagnosis of neurosyphilis were reviewed by DIERCKS (1957). ORBAN (1957) stressed the importance of the cerebrospinal fluid examination and TEODORESCU *et al.* (1958) the need for such an examination during the third year following treatment of early syphilis. Some 8% of a group of paretics reported by LOCOGE and CUMINGS (1958) had a negative Wassermann reaction in the spinal fluid and a positive reaction in the blood. That a recent course of penicillin given for any purpose might have masked the spinal fluid findings when found to be normal in GPI was suggested by MACKENZIE-VAN DER NOORDAA and HAAGSMA (1958). In Vancouver clinics the colloidal gold reaction has been found to give less reliable results than the cell count and protein estimation and its use has been discontinued (*Bull. Vancouver Med. Ass.* 1958).

In the treatment of GPI HAHN *et al.* (1958) reported that the trend was towards penicillin alone and as a routine the employment of the probable additive effects of fever were not justified. Fever therapy was considered by MARESCHAL and NOBLET (1958). Treatment with 300,000 units of penicillin daily to a total dose of 6–12 mega units was used on 51 patients and with fever in addition in 25 others by TEMPSKI *et al.* (1957), who claimed better results when both were given—as did DEGKWITZ (1957) reporting a series of 56 cases.

That cortisone might favourably influence the lightning pains of tabes dorsales was suggested by DE GRACIANSKY and GRUPPER (1957); GARDE and VIALA (1957) gave hydrocortisone intrathecally in two such cases.

### *Congenital syphilis*

BURGESS (1958) reported a case in which a macerated foetus was born at the 27th week, 4 weeks after a penicillin course had been given to a syphilitic mother. Treatment could have been given earlier in this case and prompt treatment is therefore recommended.

Asymptomatic congenital syphilis was considered by ORLANDO (1957) while PUTKONEN *et al.* (1957) studied the passage of antibody from mother to child in 213 infants and concluded that the complement-fixing antibody was by no means always more easily passed than the flocculating antibody.

Asymmetry of finger length as a possible symptom of congenital syphilis was considered by RÖSLER HANS DEITER (1958), and a gumma of the liver in a congenital syphilitic male of 6 years by WHITEHOUSE and MACFARLANE (1958). A case of aneurysm of the aorta in a 20-year-old congenital syphilitic patient was described by BEARD and THOMPSON (1958).

Congenital syphilis as a cause of mental deficiency received attention from COURVILLE (1957). Epileptic fits were noted to occur in 14 of 924 congenital syphilitics in India by SAHU (1958); penicillin was claimed to be effective in this condition.

A case of nerve deafness treated successfully with prednisone and penicillin was reported by MURPHY *et al.* (1958). EISENSTEIN and TAUBENHAUS (1958) described Cogan's syndrome (non-syphilitic interstitial keratitis with vestibulo-auditory symptoms which may be associated with systemic, especially cardiovascular, disease). Only 23 cases could be found in the literature.

The relationship of interstitial keratitis to trauma was considered by VOISIN and POULIQUEN (1957), and ASHWORTH (1958) described a follow-up of 84 eyes of 50 patients with interstitial keratitis treated with local cortisone therapy. Such treatment was considered to give good expectation as regards visual acuity and little or no corneal scarring. The presence of corneal vascularization did not affect a good prognosis.

In Munich CAILLOUD and WELLER (1957) used 100,000 units/kgm. of benzyl penicillin daily in 6–8 oral doses for 14 days on 95 babies with congenital syphilis. There were 5 deaths (2 on the day following admission, one after 6 weeks from tetany, one with dyspepsia on the 11th day and one from intercurrent infection). About 1/3 of cases had a febrile Herxheimer reaction.

## Serology of Syphilis

### *General*

Progress in serology was reviewed by CORONEL (1958), KNOLLE (1957), HEYMANN (1957), JORDAN and FEGELER (1957) and by TEAGUE (1958).

The formation of lipid antibodies in syphilis was considered by FUHNER (1957) and by MIKOL (1958). CHARTOL (1958) reported that in Africans the blood lipids were increased in early and decreased in late syphilis. The phospholipids were increased in all cases and decreased more slowly with treatment. A battery of serum protein tests was done on 91 patients with syphilis by WOLF (1957); abnormalities before and after treatment were found in about 10%. The behaviour of serum protein lability reactions and electrophoretic findings following the treatment of syphilis were described by WOLF (1957). That aqueous humour shows positive reactions to tests for syphilis similar to the blood was indicated (by means of the Chediak test) by ALAERTS (1957).

The use of passive haemagglutination in syphilis was described by GALLEGO CAPILLA (1957). Anticomplementary sera were considered by LINDER and BRUN (1957) and by ORIO and VARGUES (1958) who found 3·7% of anticomplementary results in Africans compared with 1·2% in Europeans.

Technical problems in the preparation of syphilis antigens received attention from SCHNEEWEISS and PRZYBOROWSKI (1958).

*Conventional serum tests*

The quantitative determination of complement was described by SCHNEEWEISS (1957).

In the far north of Russia sheep and guineapigs are difficult to breed. DEMCHENKO (1957) reported a modification of the Wassermann reaction in which erythrocytes from polar deer and haemolytic serum from immunized rabbits were used. LAURELL and LINDAU (1957) studied the electrophoretic mobility of Wassermann reagins from negative to positive in two female patients infected with syphilis from the same man. Compound complements for the Wassermann reaction in guineapig and swine serum were considered by MANSKI and KIELCZEWSKA RDULTOWSKA (1958). The use of filter paper chromatograms for reading the results of the Wassermann and other tests was described by ITO (1958).

That the veronal buffer increased the sensitivity of the Kolmer test was emphasized by SINNECKER (1958). RATNATUNGA *et al.* (1957) described the use of the Price precipitation test in Ceylon. A standard complement-fixation test was described by DE BRUIJN (1958) and the Roulin complement-fixation test by ROULIN and BAELDEN (1957).

A slide modification of the standard Kahn test was considered by SEN and RAO (1958), the Kline test by BOLGERT *et al.* (1958), and a modified VDRL test by TANNEN (1958), who used a finger prick method.

The rapid plasma reagin test was described by SCHMIDT and BENTZON (1958) and over 3,000 tests on dried blood were made by SANDER (1958).

*False positive reactions*

False positive reactions to reagin tests were considered by GOSPODINOFI and CARLIZZA (1957) by MILLER (1958), and by LACHOWICZ and ROZNIECKA (1958).

HARRIS *et al.* (1958) reported that false positives to reagin tests (and to treponemal complement-fixation tests as well) were more common in females than in males, and CANNON (1958) indicated a possible inheritance factor in recording a family of father, mother, 2 sons and 3 daughters in which all the females were reactive in this way.

The mechanics of false positive reactions in disseminated lupus erythematosus and other diseases were considered in much technical detail by GAJDUSEK (1958) and by MACKAY and GAJDUSEK (1958). Of 108 smallpox convalescents examined by COLLARD and EVANS (1958) in Nigeria 34 (31·5%) gave positive reactions to the Kahn test compared with only 8·5% of 2,257 adult male blood donors in the same area.

False-positive reactions in leprosy were considered by ZARCO and CHAN (1958), who found 52·7% of 108 subjects reactive to the Kahn test, 26·8% to the VDRL slide test and only 3·7% to the VDRL complement-fixation test, whose results showed excellent agreement with those of the treponemal immobilization (TPI) test. The use of the TPI test in leprosy to distinguish false-positive serum reactions for syphilis was described by ROSETTI *et al.* (1958), and by ROLLIER (1958) in lepromatous leprosy, including the use of the TPI test. False reactions were not related to quantitative modifications of gamma globulin or to paragammaglobulinaemia.

*Cardiolipin antigens*

The first major move towards greater specificity of serum tests for syphilis was the introduction of standardized cardiolipin antigens which continue to give good results in conventional serum tests. ROULIN and BAELDEN (1957) compared a cardiolipin complement-fixation test with the treponemal immobilization (TPI) test. They found the two tests equally sensitive, but the TPI test was more specific. The use of cardiolipin antigens in tests on cerebrospinal fluid was described by CHACKO *et al.* (1957).

The composition of cardiolipin is discussed by RICE (1958), who considered that it is not a single compound but a mixture of similar compounds varying in fatty acids. The preparation of cardiolipin was described by FAURE and MORELEC-COULON (1958), and the effects of variations in the lecithin component were discussed by KENT *et al.* (1958) and by REYN and BENTZON (1958).

*Treponemal antigens*

A striking development of recent years has been the discovery of antibodies other than reagin which can be detected by means of specific antigens derived from spirochaetes.

Tests with virulent *Trep. pallidum* (Nichols strain) as antigens include the treponema immobilization (TPI) test, the treponema pallidum methylene blue test [the affinity of virulent treponemes for methylene blue is lost when they are incubated with syphilitic serum and complement], the treponema pallidum complement-fixation test, the treponema pallidum immune adherence test and the treponema pallidum agglutination test. The most recently evolved tests use the avirulent Reiter strain for complement-fixation tests either as the whole spirochaete or as a protein extract. Skin tests, which seem to depend for their action on similar antibodies, are also available.

Treponemal serum tests in general were considered by BROWNE and COFFEY (1958) and by KITTNAR *et al.* (1958). BÉNAZET *et al.* (1958) stated that treponemal antigens were superior to lipid antigens and those prepared from non-pathogenic organisms were superior to those prepared from pathogenic strains—a view shared by WHEELER *et al.* (1958). A possible reason for this is that the non-pathogenic strains (Reiter) may be cultured in the pure state whereas the virulent organisms are obtained from rabbit testicles and the antigen may therefore contain some testicular tissue.

### *Treponemal immobilization test*

The TPI test was considered by FRIBOURG-BLANC (1957, 1957a); HARDY (1958); DELACRATEZ (1957); VINCENT (1957); PAGES and MANY (1958) and by MUSCHEL *et al.* (1958). Its results in GPI were described by DA FONSECA and RAMOS (1957). Its use in experimental syphilis was considered by BERLINGHOFF (1957a).

Measures to increase the sensitivity of the TPI test were described by ROSENAU and KENT (1958). The sensitivity was increased, stated MILLER *et al.* (1958), by diluting the medium so that there was only one spirochaete per field. As this was impracticable for routine practice 5 spirochaetes per field were recommended. The use of double the amount of serum in cases showing doubtful results was suggested by BONCINELLI *et al.* (1957).

The TPI test in relation to the survival of *Trep. pallidum* in human serum was described by BELLONE and BONELLI (1957). A time-saving method of preparation of the medium of the TPI test was outlined by FUCHS and AHRENS (1958) whereas BOREL *et al.* (1958) and GASTINEL *et al.* (1958) found lyophilized (freeze-dried) medium excellent as able to give constant results. The use of international control sera for stabilizing the results of the TPI test was described by KRAG *et al.* (1956).

BARNISKE (1957) described 3 years of experience with the TPI test; in untreated syphilis it remained positive whereas the conventional serum reactions might ultimately become negative. PERASON *et al.* (1958) described the use of antigenic stimulation of suspected syphilitics with negative TPI tests by injection of killed *Trep. pallidum* while FIUMARA and HILL (1958) presented the cases of a TPI test being positive in the mother of a congenital syphilitic patient and also in the wife of a man with secondary syphilis—both of whom had negative reactions to reagin tests. Diagnosis is rendered more difficult if, for any reason, the syphilis has previously been treated with penicillin in inadequate doses.

Even with the TPI test false results may occasionally occur but DUREL (1957b) considered that the figure of 8% of false-positive readings (previously given by Kolmer) was too high and that unsuspected previous syphilis, or other treponematosis—*e.g.* yaws—might explain many of these cases.

That herpes zoster might reactivate a TPI test result in a treated syphilitic patient was indicated by THIERS *et al.* (1958a).

### *Treponema pallidum complement-fixation (TPCF) tests*

The treponema pallidum complement-fixation test, in which the Nichols strain of virulent *Trep. pallidum* obtained from rabbit testicles is commonly used, was described by BERLINGHOFF (1957b), GUYON and COLE (1957) and by VACCARI (1957). HARRIS *et al.* (1958) found agreement between the TPCF and TPI tests in 87·3% of 2,000 sera.

PRICE (1958) used mechanically disintegrated *Trep. pallidum* as an antigen for the Wassermann reaction on 7,930 sera and 505 specimens of cerebrospinal fluid. The test became positive in early syphilis sooner than the TPI test but was more sensitive than the TPI test in coloured patients. The treponemal Wassermann reaction responded more quickly to treatment with penicillin than did other tests.

### *Reiter protein complement-fixation test*

That the Reiter treponemes have a common antigen with pathogenic treponemes was indicated by DARDANONI and CENSUALES (1957). Although *Trep. pallidum* is destroyed by lyophilization the Reiter treponeme is not (GASTINEL *et al.* 1958). A complement-fixation test can be made with a suspension of the Reiter treponeme (Pallignost) as antigen, or a disintegrated suspension (Pallida), or a protein extract of the Reiter spirochaete.

The Reiter treponeme is not suitable for the TPI test but by ultrasonic disintegration of this treponeme the Pallida antigen is prepared. Its use has been described by JENEY *et al.* (1957) and by RUGE *et al.* (1958) who performed 1,000 tests at Kiel; it is, however, relatively very expensive.

The Reiter protein grows *in vitro* and a soluble protein extract can be prepared from it and used in complement-fixing procedures. GASTINEL *et al.* (1957) claimed that as regards sensitivity the results of tests with the protein extract antigen were equal to those obtained with a suspension of the Reiter treponeme, the manipulation of the test being much easier. Using the protein extract BÉNAZET *et al.* (1957) reported only 0·6% of non-specific reactions on 751 sera, compared with 3·0% when a suspension was used. Its specificity was also good. FOSTER *et al.* (1958) found it more sensitive and more specific than the standard Wassermann reaction on 1,000 routine cases, and very suitable for routine use—a view shared by KOSTANT and KELCEC (1958). Other papers on this test include those of BOSSAK *et al.* (1958) who performed the Kolmer test with Reiter protein antigen and of MILLER *et al.* (1958a) who compared the Reiter protein complement-fixation test with the TPI test and had 97·8–100% of agreement.

The preparation of the Reiter protein antigen was described by DE BRUIJN (1957) DE BRUIJN and BEKKER (1957) and by WALLACE *et al.* (1958). It was easily prepared in the average laboratory at less than 1 cent for a test dose and proved reasonably stable.

### *Agglutination tests*

The treponema pallidum agglutination test was considered by CAIN (1957). HIPPIUS *et al.* (1957) used this test on the cerebrospinal fluid of 59 patients with neurosyphilis and found agglutinating antibodies in 56%.

### *Immune adherence test*

FEGELER (1957) compared the immune adherence test with the TPI test on sera from 249 untreated syphilitics. The immune adherence test was slightly less reliable than the TPI test but the immune adherence test was easier to handle as killed spirochaetes were employed.

### *Skin tests*

ROTTMANN (1957) propounded the theory of focal syphilis in which viscera, the nervous system and blood vessels were principally attacked. He described the repeated use of the Luotest (a skin test with an extract of syphilitic rabbit testicles) on 45 patients and noted that a negative serum test for syphilis might become positive after skin testing in this way. GRILLMAYR (1957) applied the skin test to a large number of patients at the Island Clinic, Colombo, Ceylon. He coined the term "island disease" for focal syphilis manifested by symptoms often mistaken for hysteria or schizophrenia.

### *Other tests*

A fluorescent test for treponemal antibodies was described by DEACON *et al.* (1957). The Reiter treponeme has at least 4 antigen components and a further antigen, a lipopolysaccharide, is currently under investigation by D'ALESSANDRO and DEL CARPIO (1958). A haemagglutination test with Reiter protein soluble antigen was described by LAMEDICA and ROBERT (1957).

## **Treponematoses**

### *Endemic syphilis*

The epidemiological aspects of endemic syphilis were considered in detail by GUTHE and LUGER (1957), and HUDSON (1958) has written a book on a sociological and medical study of bejel, the endemic syphilis of Syria and Irak. The same author (1958a), believing syphilis and yaws to be the same disease, preferred the term "Treponematosis" to "Treponematoses". LUGER (1958), also wrote on endemic syphilis in Syria where 49,000 persons of 130,000 examined in a mass campaign during 1954–56 were found to be infected. He suggested that the absence of visceral involvement might be explained by heightened immunity resulting from repeated subclinical superinfections. The sociological conditions in relation to endemic syphilis in this area were considered by LUGER *et al.* (1958).

ILIC and IGNJATOVIC (1957) described the successful mass campaign against endemic syphilis in 50 districts of Serbia (population 1·5 millions which also included persons engaged in navigation on the Danube river). ILIC (1957) reported that a combination of penicillin and bismuth was no more successful in its control than penicillin alone.

MURRAY (1957) reviewed the South African literature concerning endemic syphilis and yaws. He concluded that the Bantu did not suffer from syphilis prior to contact with Europeans. There was no syphilis early in the 19th century but the disease had become common by 1881, the opening of the Kimberley diamond mines having contributed markedly to its spread.

### *Yaws*

The epidemiology of yaws was considered by HACKETT (1958) and the same author (1957) presented a useful illustrated book defining an international nomenclature of yaws lesions. The clinical aspects of yaws were considered by HASSELMANN (1958). Resemblances between yaws and leprosy were outlined by DAVEY (1957).

Yaws-like lesions in Uttar Pradesh, India, were described by PRABHAKAR (1957), and 124 cases of yaws in Hankow, China, among a mainly floating population situated in an area north of the tropical zone, by YU (1957). The epidemiology of yaws in two islands of the Zanzibar Protectorate was considered by TALLACK (1957), and yaws in S. W. Borneo by VAN DER HOFF (1957). A short history of yaws in Trinidad was presented by FAWKES (1957), and GENTLE (1957) discussed it there, in reference to seropositivity. Of 27,231 blood specimens examined 26·3% were positive to yaws or syphilis. MIKOL and SOLENTE (1958) failed to differentiate late syphilis from late yaws, using the Kahn universal reaction.

According to a report presented to the Executive Board of the World Health Organization (*Med. J. Australia,* 1958) eradication of yaws is possible within 10 years. By the end of 1958 no less than 100 million persons had been examined in the WHO mass campaigns and 25 million treated with penicillin. The bulk of the remaining cases were in Africa. Mass campaigns were in progress in Indonesia, Thailand, Malaya, Laos and the Pacific Islands. In Haiti the prevalence had been reduced from 36·5 to 0·57% and in Western Samoa from 11·0 to 0·04%.

BERTE and LINHARD (1957) reported on syphilis serology in Africans in areas where other treponematoses (*e.g.* yaws), and false positive reactions might confuse the diagnosis. When 4 tests were done on 1,024 blood donors in 596 the results were uniformly negative, in 325 uniformly positive and in 103 (10%) difficult to interpret.

In Eastern Nigeria the mass campaign (based as most are on the use of procaine penicillin with aluminium monostearate) has also been strikingly successful. The prevalence of active yaws has been reduced from 17 to 0·7% and of infectious yaws from 5 to 0·36% (WHO 1957).

Penicillin given orally and bismuth given orally and by injection in yaws were considered by FRIEDHEIM (1957). In Brazil the campaign based on benzathine penicillin has been described by DE AQUINO (1958) who noted also the responses of patients given intradermal injections of material obtained from papillomata and raised the possibility of immunization against yaws by means of vaccination. GUIRAUD (1958) used placental "cubes" locally in 35 cases of yaws osteitis with discharging fistulae. The use of placental tissue as a dressing has been known to the Chinese for 5,000 years.

*Pinta*

The epidemiology and symptomatology of pinta in Mexico were described by CASTELLANOS and GONZALEZ PINON (1957). BECKER and HILL (1957) investigated 24 cases thought to be pinta in British Honduras; the spirochaete was not, however, found in any and, although the signs were suggestive, the presence of pinta remained unproven. WHEELER *et al.* (1957) reported that the new antibiotic Synnematin B (Cephalosparin N) had been noted to cure 2 cases of pinta in Mexico when being used in the treatment of typhoid fever.

## Venereal Disease Control

*General*

The WHO Western Pacific Regional Seminar on venereal diseases held in Tokyo in March 1958 has been reported (*Lancet* 1958) (WILLCOX 1958a). The activities of the British Federation against the Venereal Diseases have been reviewed by NICOL (1958a).

*U.S.A.*

Syphilis control in upstate New York was considered by THOMAS (1957) and VD control in Texas by DOANE (1957).

That syphilis remains a problem in U.S.A. is emphasized by BEERMAN (1958) and HECHT (1957) threw considerable doubt as to whether the venereal diseases were really conquered. FIUMARA (1957) expressed the view that syphilis could never be entirely eradicated. THOMAS (1958) noted that over 200,000 new cases of syphilis were reported in U.S.A. even in 1956 and GELPERIN (1958) indicated that over a million cases of gonorrhoea were still occurring annually there, of which 20% were in the so-called "teenage-group" (15–19 years) which occasioned much cause for worry. Similarly, TALBOT and O'NEILL (1958) reported that while both syphilis and gonorrhoea had decreased in Connecticut in 1957 there was a 116% increase of syphilis and a 64% increase of gonorrhoea among teenagers. Gonorrhoea was also increasing in Nebraska, especially in teenagers (PARKER 1958).

*Europe*

In the clinics of England and Wales in 1956 the numbers of cases of early syphilis rose from 837 to 844, an increase for the first time since the war (17,675 cases in 1946). The numbers of cases of gonorrhoea rose much more sharply to 20,388 from 17,845 the previous year (17,536 in 1954), and of non-gonococcal urethritis to 14,825 from 14,269, continuing an uninterrupted rise from 10,794 cases in 1951 (*Brit. J. Venereal Dis.*, 1958). It was obvious, stated KING (1958), that the venereal diseases were not "dying diseases". The earlier decline had been due more to better social conditions than to new remedies, he wrote while presenting strong arguments to encourage young men to enter the field of venereology. Recent developments in venereal diseases in Eire were considered by LANIGAN-O'KEEFFE (1957).

In France too there has been a slight recrudescence of early syphilis since 1954 (*Postgraduate Med.* 1958; TOURAINE 1958) where, reported TOURAINE (1957), there was still a 1% seropositivity rate and venereal diseases remained a substantial problem.

The dissemination of venereal diseases in West Berlin over a 10-year period was described by KREBS (1958). In Poland an increase of syphilis was reported in the Gdansk area (MIEDZINSKI and MARKIEWICZ-SZUMSKA 1957) and in the Silesian health resort of Cieplice (KOLANKOWSKI 1957). In Seville, Spain, high seropositivity rates still prevail. MORALES *et al.* (1957) found 23% of sero-positive readings in 227 pregnant women and positive findings were also noted in 63 of 531 schoolchildren.

In Hungary, on the other hand, KAROLYI (1957) indicated that between 1947 and 1956 the annual numbers of cases of early syphilis had declined from 15,061 to only 37, of gonorrhoea from 37,496 to 7,544 and of soft sore from 1,675 to 35. In Switzerland the current syphilis rate was assessed by FISCHER (1957) as 0·5 per 1,000 compared with 0·5% in 1920.

*Other areas*

In many other parts of the world the venereal diseases continue to show high prevalence. A pilot study of venereal diseases among the Bukoba tribe of Tanganyika was described by LAURIE (1958), who urged that the World Health Organization should be asked for assistance. Seropositivity rates in the Upper Volta region of French West Africa were discussed by CHARTOL (1958). In Leopoldville in the Belgian Congo BRUAUX *et al.* (1957) reported that the annual gonorrhoea rate was 28 per 1,000 and the sterility rate was 9%. In Algiers MARRILL and ZERBIB (1958) stated that the histories of 14% of patients gave some indication of syphilis. The serum findings during a mass campaign in Morocco were described by MAURY and WEBER (1958).

In Bombay, India, in 1950 there were 37% of positive findings in 9,226 serum tests made on patients in clinics and hospitals. Of 16,059 tests made by MUNGALE *et al.* (1958) in 1956 the positivity rate was still 21·3% Of 1,176 new patients attending the venereal disease clinic at New Delhi TAMPI and RAO (1958) reported that 68·5% were married. In Mexico seropositivity rates of up to 19% were noted by RAMIREZ *et al.* (1958). Venereal diseases problems in the Western Pacific Region were reviewed by WILLCOX (1958a).

*Prostitution*

GRYSON (1957) indicated that Belgium had some 50,000 prostitutes per 9 million inhabitants although prostitution was legally abolished. ROSENTHAL and VANDOW (1958) compared the findings in prostitutes arrested in New York in 1950–56 with those of 1936–46. During the more recent period the prostitute played a lesser role in the spread of venereal disease than did the promiscuous amateur. There had been a decrease of 49% in the number of prostitutes arrested between 1940 and 1956 but an increase since 1952. Between 1942 and 1946 some 186 cases of infectious syphilis had been found but only 5 between 1952 and 1956. In 1956 only 5·2% of prostitutes had gonorrhoea compared with 23·6% in 1946. The seropositivity rate of 22·7% in 1946 had decreased to 4·0%

by 1954 but had increased again to 10·5% in 1956. In West Berlin, on the other hand, Grimm (1958) reported that 19·4% of destitute women and 15·7% of persons received by the police had venereal disease.

That seropositive prostitutes were contagious for syphilis before signs of secondary syphilis appeared was indicated by Garnier (1958). In Paris Durel (1958) was conducting a study of 200 prostitutes who were being given 2·4 mega units of benzathine penicillin each month.

### *Homosexuals*

The relatively high incidence of syphilis in homosexuals, as the disease has receded in the remainder of the population, is evident. Degos (1958), in France, stated that in 1950 pederasty was responsible for only 2–4% of syphilitic infections but by 1954 the proportion had increased to 10%. Goodman (1957) stated that of 428 cases of new syphilis 10% were in homosexuals. He reported that 9 young men who had been exposed to each other all had infectious syphilis. Marmell (1958) reported that homosexual practices were admitted in 44 of 48 cases of granuloma inguinale of the anus reported in the literature.

### *Migrants*

Laird (1958) noted that one-half of the gonococcal infections seen in Manchester, England, occurred in persons born outside the United Kingdom. West Indians and West Africans were responsible for one-third and citizens of Eire for about one-fifth: nearly one-half the patients admitted previous infections with gonorrhoea. In the U.S.A. about 400,000 Mexican agricultural workers cross the border in each year in search of work. The physical examination given to them was considered by Smith *et al.* (1958) to be a useful measure of VD control. Ackerman and Donaldson (1957) reported that 8·6% of 6,273 agricultural workers in Florida had positive serum tests for syphilis.

The Agreement of Brussels, the basis of international cooperation concerning venereal diseases in seamen, and now administered by WHO, has been studied by a World Health Organization Study Group (WHO 1958); a broad international approach to the whole health problem of seafarers is recommended.

### *Case finding*

Much venereal disease is seen in the first instance by the general practitioner who has an important role in VD control (Nelson 1957); Taggart (1958); Thomas (1958a). The diagnosis of venereal diseases in general was considered by Mascall (1958).

The use of routine blood tests is an important case finding procedure for syphilis. But as syphilis becomes less and less prevalent the procedure becomes less economical when expressed as cost per case of syphilis found, and there is a tendency to relax the enforcement of such tests.

Thus in 1958 the Joint Commission of Accreditation of Hospitals in the U.S.A. dropped the previous regulation of a routine serum test for syphilis on patients admitted to hospitals, a fact deplored by Rosahn (1958). Hedrich and Silverman (1958) considered that compulsory premarital blood tests were no longer necessary and, as the decrease of syphilis had been similar in compulsory and non-compulsory areas, the measure had not contributed materially to the fall in the prevalence of syphilis. Premarital blood test requirements in Indiana were considered by Van Fleet (1957).

There is thus a tendency, in using mass serum testing as a case-finding tool, to concentrate on sections of the population more than usually prone. Thus Rosenthal and Vandow (1957) reported that 14·4% of seroreactors were found in 23,675 persons tested in a house to house survey in Harlem, New York, in 1955.

Of all the methods of case-finding the epidemiological method of contact tracing was considered the most valuable by Dumitriu *et al.* (1958). Increased case-finding activities of all kinds in Portland, Oregon (*Oregon Health Bull.* 1958), had increased the syphilis morbidity by 300% and the gonorrhoea morbidity by 251%, which figures compared with 29 and 52% respectively in the rest of the State.

A report made to the British Federation against the Venereal Diseases (*Med. Officer* 1958) of 292 patients (231 males) attending a venereal disease clinic for the first time, indicated that only 5 had seen leaflets, 200 men had seen posters, and that sex books or articles had been read by only 85. Only 73 had received any kind of sex instruction.

## FOOTNOTE

The majority of the papers listed, or abstracts of them, were published during 1958 in this *Bulletin*, the *Tropical Diseases Bulletin*, *Abstracts of World Medicine* and/or the *British Journal of Venereal Diseases.* The author is also indebted to the Public Health Service of the US Department of Health, Education and Welfare, and to the World Health Organization, for additional information provided, especially for the *Abstracts of Current Literature* published by the former.

Where papers are by 2 authors the name of each author is listed in the text; where 3 or more authors have collaborated, the name of the first, with the term *et al.*, is used but the names of all authors are given in the list of references.

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# Public Health

MINISTRY OF HEALTH. **Report of the Ministry of Health for the Year 1957. Part II. On the State of the Public Health being the Annual Report of the Chief Medical Officer** [CHARLES, J. A.]. Cmnd. 559. pp. vi + 292. 2 diagrams, 4 figs. & 2 graphs. 1958. London: H.M. Stationery Office. [13s.]

This volume maintains the high standard set by its predecessors [for a review of the report for 1956 see this *Bulletin*, 1958, v. 33, 426]. It contains 30 more pages and costs 4s. more. There are new chapters on the Care of Young Handicapped Children and on Accidents in the Home. One entitled Care of the Aged with Mental Illness replaces that on "Care of Old People". The chapter on General Public Health is recast. Mental illness is a recurring theme due to consideration in the department of the report of the Royal Commission on the Law relating to Mental Illness and Mental Deficiency [this *Bulletin*, 1957, v. 32, 961].

Sir John Charles describes in a masterly summary the high-lights of the year and in such a way as to impel the reader to seek further detail in the body of the report. Dr. Balfour KIRK is, as before, the General Editor.

The crude death-rate was 11·5 per 1,000 of the population: the birth rate 16·1: the rate of infantile mortality, 23·1 per 1,000 births: the neonatal mortality, 16·5: the stillbirth rate, 22·5 per 1,000 live and stillbirths and the perinatal mortality, 36·2 per 1,000 total births. The maternal mortality excluding abortions was 0·39, and that from abortion was 0·08, per 1,000 births.

Deaths from diphtheria numbered 6; from poliomyelitis 255; tuberculosis 4,784; bronchitis 26,935; cancer of the lung 19,119; influenza 6,716 and coronary disease 76,324.

"Noteworthy Outbreaks" of epidemic disease deal this year with smallpox, tetanus and influenza. There were 4 cases of, and 2 deaths from, smallpox. It is the usual story of a man returning from abroad, this time West Africa, and thought to be suffering from chicken pox. The tetanus outbreak, 5 cases and 2 deaths in a hospital in the Midlands, was considered to have been due to the use of infected, but inadequately sterilized, rubber operating gloves. The influenza epidemic was caused by an Asian variant of influenza virus A. There is a full account of the spread of this type of virus throughout most of the world and of the steps taken to prepare in time a vaccine against the disease. Other epidemiological data include a quite fascinating account of the tracking down of a typhoid carrier in West Mersea: the set-backs in the production of a British poliomyelitis vaccine and the considerable use made of Salk vaccine imported from the U.S.A. and Canada: altogether, by the end of 1957, 1,398,336 children had received 2 doses of vaccine and 134,821 one: the protection against paralytic poliomyelitis given by 2 doses of vaccine is estimated to be about 80%: the Public Health Laboratory Service reports that by the time the first case of poliomyelitis is diagnosed in a family the virus is already widely distributed throughout the household concerned: in certain outbreaks of streptococcal sore throat a nephritogenic strain has been isolated and the use in these circumstances of penicillin prophylactically is mentioned with approval: meningococcal meningitis still gives rise to over 1,000 cases a year of which nearly 20% are fatal: in many areas infectious syphilis is less prevalent but gonorrhoea is on the increase.

The yield of active cases of pulmonary tuberculosis from mass miniature radiography is now only 1·9 per 1,000 examined compared with 4·4 in 1946.

The introduction contains a cautious comment on recent trends in the psychiatric field and this is developed by Dr. Walter MACLAY in a balanced chapter.

In the chapter on General Public Health there are sections on clean air, water supplies, the need to avoid fragmentation within a health department and the opportunities for research.

The maternal and child welfare services receive adequate treatment and include a long section on prematurity.

The new chapter on handicapped children stresses that in the background of every such child there is a handicapped family: it describes the truly remarkable developments in recent years in the reablement of young people afflicted with various handicaps.

The background of the national scheme for obtaining information about the diagnoses of the illnesses from which hospital in-patients suffer is given: the coverage is now almost complete. The value of the results to hospital administrators and public health workers cannot be overstated.

There are the usual statistical tables.

An index would be useful in a report such as this which covers every branch of social and preventive medicine and where the chapters are drafted in the various sections of the department. Different aspects of the same topic are inevitably to be found in several sections and an index would help the diligent reader to piece them together. It would, also, help to ensure agreement about the figures: for example the deaths from poliomyelitis are stated to have been 226 on page 26; 227 in the table on page 257 and 255 on pages 6 and 54.

As has been said of previous reports both this and Part I of the Annual Report of the Ministry of Health are essential reading for all engaged in public health work.

*Allen Daley*

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MEDICAL OFFICER. 1959, Jan. 30, v. 101, No. 5, 61–8. **Public Health Functions in Greater London—I. Evidence submitted to the Royal Commission on Local Government in Greater London by the Medical Officers of Health of District Councils in the Area.** 61–3. **II. The Case submitted to the Royal Commission by the Counties Concerned.** 63–8.

This interesting series of documents follows the expected line.

The first is a composite statement by the officers of the 2nd tier authorities, that is the district councils, criticizing the alleged shortcomings of the present administrative structure and affirming that they and their authorities could do the job better. The second comprises separate statements by the 6 Metropolitan County Councils asserting in each case that their administration and services are efficient. Most say categorically that any transfer of function to other authorities would be to the detriment of the services. The County Officers are silent, presumably on the ground that these matters are high policy on which officers should not express their individual or collective opinions in public.

For the general reader, uninterested in enlarging, or disposing of, an empire the main point of concern will be facts about the right size of authority to administer the various health services. These papers make many assertions but few proposals. The facts given relate almost entirely to the present structure and how well it works, as the County Councils affirm, and how ill as the 2nd tier officers claim.

The argument of these officers is that local services must be administered really locally, that the local Town Hall and not the distant County Hall is the place at which the public expect to receive help from the health services and that a maximum population of about 200,000 is right for this purpose as it ought to have adequate financial resources and yet enables the medical officer of health to know personally all his staff and all the doctors working in the area. They do not oppose 1st tier authorities as such but they think that there need be only one for the whole of Greater London and that its functions should be limited to "those which it is essential to administer over a wide area" such as sewage disposal, the ambulance service, higher education, town and country planning and the promotion of legislation for the area. In their opinion the 2nd tier authorities should have responsibility for the environmental health services, the school and mental health services, the personal health services under the National Health Service Act which include health visiting, midwifery, maternity and child welfare, home nursing, domestic help, vaccination and immunization, health centres and after-care. They advocate close liaison with the hospital service by the appointment of the local medical officer of health to the staff of the local hospitals. They state the defects of the present organization in general terms only but offer to supply specific instances. They do not blame the 1st tier authorities for these defects but say that it is the structure as laid down by Parliament which is wrong.

The County Councils had, apparently, not seen the officers' document when their own evidence was prepared but they are unanimously of opinion that their organization does give, by divisional and area committees in which the county council members are in a minority and, in most cases, by the use of 2nd tier medical officers of health as part-time county officers, adequate attention to local needs. The Middlesex document refers to the unevenness of the district services before they were transferred to the county in 1948 and that the county has, since then, built them up where they were weak. The counties of Middlesex, Essex, Herts., Kent and Surrey all draw attention to high proportion of their population, acreage and rateable value which is within the "Greater London" area being considered by the Commission and imply that they would be crippled in their administration if these portions were separated and only the extra-metropolitan part remained.

Most of the counties refer to their ability to attract efficient senior professional staff and to expand specialist services, to help out in emergency areas where staff is required and to make large and advantageous contracts for supplies and services. Surrey states that any defect in the present services is due to the divorce of the hospitals from local government and "no increased efficiency, economy, or other public advantage will accrue either to Metropolitan Surrey or the rest of the county from the severance of the Metropolitan part from the rest; indeed, there would be definite disadvantages from such proposal". So, in other words say the other 4 counties which abut on the county of London. The London County Council itself feels that all that is needed can "be achieved through transfer or delegation of powers by ministerial orders or local Acts". *Allen Daley*

EWAN, James Twaddle Gordon. [M.B., Ch.B., D.P.H., D.P.A.]. **The School Health Service.** 112 pp., 4 graphs (3 coloured) & 7 figs. [1957.] Glasgow: Health and Welfare Committee, Corporation of Glasgow.

Dr. Ewan is the Principal Medical Officer of the School Health Service of Glasgow. That service now approaches its 50th year and the book describes why, how and when the service started and its step-by-step development and gives comparative figures to show the improvement in the health of the City's schoolchildren.

The service came into being on the recommendation of the Royal Commission on Physical Training (Scotland) 1903.

Statutory authority for it dates from 1908 but there had been a tentative beginning before then. The first, activity was routine medical inspection but this was soon followed by the provision of treatment, of feeding and clothing for the necessitous and an extensive range of special schools for the handicapped.

From 1919 the central supervision of the service has been in the hands of the Scottish Board of Health and there is complete integration with the other local health services.

In 1927–8 a special enquiry demonstrated the value of milk as an article of diet for schoolchildren: a surprising fact which emerged was that separated was as valuable as whole milk. Now each child is offered one-third of a pint of tuberculin tested pasteurized whole milk and 86% take advantage of it. Nearly 65,000 meals, mostly dinners, are served each school day at very cheap rates and even these are remitted if the income is low. The average height and weight of the children have increased steadily decade by decade. Boys of 13 are now 15·3 lb., and girls 17·3 lb., heavier than were children of that age 40 years ago.

There are 176,688 pupils in the 340 Glasgow schools of which 78, together with 11 annexes, are of open air design.

There is a full range of special schools both day and residential.

The advent of the National Health Service in 1948 dislocated the school ophthalmic service but, otherwise, the 21 school treatment centres went on without interruption. The Regional Hospital Board supplies specialists for the clinics which need them. Only 166 children were supplied with spectacles in the first year after the National Health Service took over compared with 5,577 in the preceding year and 5,537 in 1954. The Regional Hospital Board has ear-marked beds for the operative treatment of schoolchildren with adenoids and enlarged tonsils. There is an account of a follow-up survey on the value of this operation.

Glasgow, as did other large cities, got a black mark during the war because so many evacuated children were verminous and there was a high incidence of scabies and enuresis. The steps taken to cope with these complaints are described.

The school dental service has ebbed and flowed. There are now 18 school dentists and 15 dental clinics. Dental inspection is limited to certain selected schools. Emergency "toothache" cases are treated at local dental clinics daily between 4 and 5 p.m. The war-time diet had a good effect on the children's teeth: in 1930 only 15·4% had sound teeth: in 1946 it was 60·6%.

The improvement in the health of the children is impressive. In 1934 only 6·7% had no discoverable defect at routine inspection: in 1954 it was 48·1%: the incidence of rickets, once the scourge of Glasgow, was 0·3% in 1954 compared with 9·0% in 1910–14.

The author believes in routine medical inspection and will have no truck with its replacement by the examination only of children picked out by a nurse or a teacher. He would like the general hospitals to notify him of all children discharged from them as was once done by the fever hospitals.

The above are only the salient points in a report of great general interest.

The book is clearly printed and produced by the Corporation's own printing department.

The jubilee of a service is a suitable time for an evaluation of its work. One is reminded of a saying of Dr. Alan GREGG. "How subtly the past informs and influences the present and how inevitably and undeniably the present partakes of the past and will be found making up and governing the future" (*Canadian J. Pub. Health*, 1959, v. 50, 116). *Allen Daley*

HEALTH EDUCATION J. 1959, Mar., v. 17, No. 1, 1–88, 2 figs. [Numerous refs.] **History of Health Education.**

The complete issue of the Health Education Journal for March, 1959 has been devoted to 11 papers on the history of health education that "has its roots in culture, religion and social progress."

In the first paper, *Health Education in Classical Greece and Rome* (pp. 2–10), Sir John CHARLES gives an interesting account and discussion of the attitudes of the Greeks and the Romans to health and disease deduced from the writings which have survived. There are many quotations with apt comments from writings in the *Hippocratic Corpus*, the *De Medicina* of Celsus (*circa* A.D. 25) and the *Hygieia* or *De Sanitate Tuenda* of Galen. It is particularly in the *Hygieia* that much can be found on hygienic rules for the maintenance of health.

A scholarly paper, *Influenza of Culture and Art on Medical Knowledge in Renaissance Society* (pp. 11–17) by Adalberto PAZZINI is presented in translation. The author traces the development of the Renaissance, the first step towards which was the "humanism" whose roots were in the 14th century in the thought and works of Dante, Petrarch and Boccaccio. In the Renaissance, culture became more widely diffused. The author discusses the factors which caused the first germs of medical culture to be created and to flourish. His view is that art may well be an instrument in the diffusion of culture and of medical culture and in this connexion takes "Leonardo da Vinci as the most eloquent example for the marriage of artistic and scientific thought". *Health Education in the Nineteenth Century* (pp. 18–23) is the title of an article by Fraser BROCKINGTON in which he writes of the beginning of the "new health education movement" and mentions the writings of Buchan (1769), Tissot (1762), Faust (1794), Sinclair (1816), Southwood Smith (1835), Florence Nightingale (1858) and others. There came "a growing army of health educators" and then "Associations of citizens intent on public enlightenment grew up like mushrooms". The stress of the interest in health in the 19th century, however, was mainly on the individual and to some extent on vulnerable groups but "The great place which health education was to occupy in the twentieth century public health movement had not yet been realised". The paper *The Central Council for Health Education—the First Twenty-Five Years: 1927–52* (pp. 24–35) is by Sir Allen DALEY, who tells the story of the foundation of the Central Council, in which he took so active a part. Indeed, it was he who read a paper entitled. *The Organization of Propaganda in the Interests of Public Health* at a meeting of the Society of Medical Officers of Health in March 1924 in which the main emphasis was on the need for a central organization. The interest which this aroused led, after vicissitudes, to the establishment of the Central Council for Health Education. The author describes in characteristic fashion how he came to realize the need for cooperation of the public in efforts to improve the public health when he was MOH of the County Borough of Bootle from 1911 onwards and the measures of local health education of the people he was able to organize in Bootle and subsequently in Blackburn. The history of the Central Council for Health Education from its inaugural meeting on September 26 1927 through its growing-up and the war and post-war years to its present high status, is well told with much interesting description of the valuable work done by the Council and its individual members. *The Development of Health Education in the U.S.A.* (pp. 36–48) is by Sally Lucas JEAN. As a pioneer of the modern health education movement she relates the growth of this movement in the last 40 years. It is a long paper, with many references, in which the emphasis is on the health of the child. There are descriptions of school health services, the formation of the Child Health Organisation, the dramatic measures employed to arouse interest in health in the public and in school authorities, the part played by insurance companies and other concerns in the health education movement and of some of the numerous health agencies which have established programmes to promote health in schools.

*The Progress of Health Education in the U.S.S.R.* (pp. 49–57) by L. S. BOGOLEPOVA. In this paper there is first reference to many pioneers of hygienic thought in Russia from the eighteenth century onwards. Health education became the concern of the state in 1917, and in 1918 a special department for guidance in health education was set up in the People's Commissariat for Health. Apart from the educational work of the Red Cross and Red Crescent societies many other social organizations which promote health have been set up such as worker's commissions, army sanitary units, institutes for mother and child care, the Institute of Sanitary Culture and in 1938 the Central Scientific Research Institute of Health Education of the Ministry of Health. Many other activities exist—public sanitary inspectors were appointed in 1942 and the popular journal *Health* was first published in 1955.

*Hinduism and its Influence on Health Education* (pp. 58–62) by C. R. AMIN and *Some Observations on the Health Education Content of Buddhism* (pp. 63–65) by Jothiya DHIRASEKARA.

These 2 papers are short but are interesting in their description of the basic philosophies, tenets and injunctions of Hinduism and Buddhism as they tend to promote health particularly by fostering good personal hygienic habits.

*Health Education in Judaism* (pp. 66–71) by Bernard HOMA. In this paper the author describes and discusses the "instructions affecting the health of the individual as well as of the whole community" contained in the Five Books of Moses on which Judaism is based. With references to the Mosaic law in relation to hygiene some of the subjects which are considered are camp sanitation, "clean" and "unclean" food and the possible reason for this classification, ritual slaughter of animals, health food declared as *kosher*, circumcision, sex hygiene, the "impurities" that is the infections of gonorrhoea, of leprosy and other diseases. Moses "may be regarded as among the earliest exponents of preventive medicine and public health".

*Christianity and Health Education* (pp. 72–78) by A. J. DALZELL-WARD. The theme of this article is that "Just as the Laws of Moses have been confirmed by modern science, so also has the philosophy of Jesus, respecting the laws which govern interpersonal relationships, been confirmed by psychiatrists and social psychologists. It is in the sphere of mental health that Christianity has made its own contribution". This view is elaborated by the author by discussion of quotations from the New Testament.

*Health Education and Islam* (pp. 79–88) by KH. B. EL BEDRI. This is an interesting article in which it is first pointed out that "Islam" is the term used by the enlightened Muslim for his religion and not "Mohammedanism" for Mohammed himself was neither God nor part of God but only a prophet. The 4 foundations of Islam are stated—(1) the *Quran*—the holy book, (2) the *Sunna*—sayings and practices of Mohammed, (3) *Ijimaa*—unanimous consent of the *Ulama* (learned doctors of Muslim Law) and (4) *Quiyas*—reasoning by analogy. Sections of the article deal with Mohammed—the Educator, sex education and personal hygiene in Islam, control measures and mental health in Islam. "Islam, with its four sources, is rich in health education content."

*M. E. Delafield*

CENTRAL AFRICAN J. OF MED. 1958, June, v. 4, No. 6, Suppl., 269–80. **First Report of the Planning Committee** [FARRER-BROWN, L., Chairman] **appointed by the University College of Rhodesia and Nyasaland to advise it on the Desirability and Practicability of establishing a Medical School.**

——. 1959, Mar., v. 5, No. 3, Suppl., 145–72. **Second Report of the Planning Committee** [FARRER-BROWN, L., Chairman].

In the first report the Planning Committee concludes that the Federation will fall behind comparable communities unless it plans a medical school. The present medical services are inadequate with a shortage of medical personnel in rural areas. In 1957, 130 students (19 of them African) from the Federation were known to be taking an undergraduate course in medicine elsewhere. The doors are closing to African and Asian students from the Federation in the Universities of the Union of South Africa and weighty reasons are given against dependency on the United Kingdom for the provision of undergraduate facilities. The Committee took cognizance of the medical schools at Makerere and Ibadan, but does not detail the difficulties which might be encountered if African and Asian students from the Federation were required to travel to Uganda to obtain education at Makerere. The Committee recommends the site for the medical school to be at Salisbury and, with some reluctance, a few miles from the present buildings of the University College of Rhodesia and Nyasaland in order to be adjacent to the eminently suitable African hospital at Harari. The separation of the medical school from the main University College is regrettable, but it would be sufficiently near for the medical undergraduate to enjoy the company of his contemporaries in other faculties. It is recommended, in the second report, that the curriculum should be arranged to enable students to make yearly visits to their homes, which, in some instances, will be many hundreds of miles away. (Travelling by air to Makerere would not be very different for students from Nyasaland, for example.) The capital cost of the buildings and the recurrent costs of staffing are formidable, but the "capital which is constituted by the health of the people" must be preserved. There appears to be no acceptable alternative to a medical school in the Federation and it is hoped that education together, especially in the healing art, of undergraduates from diverse communities will help to relieve racial tensions. It is clearly essential that the degree obtained should be such as to be recognized as worthy of registration by the General Medical Council. One which was only locally recognized would never satisfy the aspirations of the undergraduate. It is appreciated that the number of Africans wishing to study medicine who possess an adequate preliminary education is at present small, but the Committee sees no difficulty in the majority of the medical students in the earlier years coming from the European and Asian communities. It believes that economic and other considerations will ensure that these students will not obtain their medical education elsewhere once the Federation opens a medical school.

The recommendations of the first report were accepted in principle. In the second report the Committee outlines an imaginative curriculum, shorn of unnecessary traditional trappings. It aims at an early intermingling of preclinical and clinical teaching. It proposes a novel examination system to test progress under such a curriculum. This should be studied in detail. The planning of the first medical school in a country where no provision has to be made for students to enter at different stages enables such a changed curriculum to be proposed with a reasonable prospect of it being workable and without disturbing students who have begun to follow more traditional programmes. The Committee suggests that some bias should be allowed to prepare students for their future work in the Federation. It might be suggested that teaching chiefly carried out in an African hospital would carry with it certain disadvantages for those whose practices may be largely among more sophisticated people enjoying a higher standard of living, but the principles of medical practice, if properly assimilated, can be readily applied in a different field and the wealth of clinical and pathological material available in an African hospital more than compensates for any shortcomings it may have in being dissimilar from that found in European communities.

It is impossible to conduct a successful medical school unless medical research is being actively pursued. Rhodesia possesses a vast number of medical problems awaiting investigation. It is to be hoped that the cost of the medical school would yield a rich dividend in the research work which would be accomplished. The gradual opening of the school would enable the clinical professorial units to start on research problems before the first undergraduates made appreciable demands on their time for teaching. The expected salary rates payable to the necessary staff are estimated. Although the work would clearly be of great interest, salary scales, amenities, security of tenure and facilities for satisfactory work would have to be generously provided to attract staff of the highest calibre and no other would be adequate for the task. The hospital service might reasonably contribute to the salaries of clinical staff and part-time teaching posts for clinicians selected for their teaching ability but already in the hospital service are envisaged. The teaching of public health and rural hygiene is of great importance and suggestions are made as to the integration in the course of family studies. Language difficulties appeared formidable to the Committee, but will probably prove to be surmountable without undue difficulty.

[Political and economic stability would assist such a scheme to achieve success, but the Medical School might well help in the maintenance of a good relationship between different communities.] *Frederick J. Wright*

KILPATRICK, J. **The Growth of an Organization for Preventive Medicine.** *Proc. Roy. Soc. Med.* 1959, Apr., v. 52, No. 4, 284–90 (Sect. Epidem. & Preventive Med. 12–18).

This Presidential Address describes the growth in outlook, approach and experience of the Medical Branch of the Royal Air Force since 1920 when its first annual report was completed. Maintenance of the health of aircrew was a prominent responsibility, but there were also general problems of nutrition, environment, climate, clothing, prevalent diseases and others. The population concerned, varying from 30,000 to 60,000 before the war and to over a million during it, was scattered widely over the world and the doctors were responsible for both treatment and preventive measures. The average measurements of recruits are reported, and the common grounds for their rejection proved to be dental and visual defects. In discussing nutrition the author mentions an investigation of the vitamin C reserve of 50 airmen in a station in Great Britain. Minor deficiency was noted in 22 and a more marked degree in 5.

Disabilities and injuries were prominent in statistical records of diseases, but sandfly fever was a serious cause of ill-health overseas, reaching in one area an incidence of 250 cases per 1,000. In 1921 a commission appointed from the Service made a careful investigation of the epidemiology of this disease and recommended measures for control; a decrease in incidence was noted after 1923. Until 1937 dysentery proved more amenable to control than malaria because routine measures were effective in the former while personal precautions were needed in the latter. Progress was made in adaptation to hot climates, but the spine pad, topee and upright collar were abandoned only slowly. The most important occupation, the flying of aircraft, was the subject of steadily improving preventive measures starting from the selection of the candidate. Research into physiological and psychological aspects of flying, through initially adequate, became too much restricted just before the war and a Research Committee was formed which enlisted the help of civilian scientists. The great expansion of the Service during the war and the dilution of the Regular personnel did not destroy the fundamental organization. It is concluded that the Service has grown up.

*T. H. Davey*

# Maternal and Child Health

SALBER, Eva J., STITT, Pauline G. & BABBOTT, Joan G. **Patterns of Breast Feeding. I. Factors affecting the Frequency of Breast Feeding in the Newborn Period.** *New England J. of Med.* 1958, Oct. 9, v. 259, No. 15, 707–13. [24 refs.]

This paper is from Harvard University and reports on the attitude towards breast feeding of 114 healthy primiparous women who attended the Family Health Clinic of the Boston Lying-in Hospital between 1950 and 1956.

The prevalence of breast feeding in the U.S.A. is the lowest of any country in the world that reports its figures. In 1956–7 75% of the infants discharged from the Boston Lying-in Hospital were bottle fed.

The 114 cases studied were self-selected rather than a random or typical sample: 32% of the mothers were college educated; 12% American Negro: 60% were born in New England States, 31% elsewhere in the U.S.A. and the rest outside America. Most of the mothers had worked before marriage and during pregnancy and, in many, economic hardship had resulted from its cessation. All had had their confinements in hospital: 93% of the deliveries were instrumental.

The percentage attempting breast feeding was 62·3. The staff tried to be neutral but expressed satisfaction when the mother decided to try breast feeding. Most mothers had made up their minds as between breast and bottle feeding some time before the child was born and any pressure, one way or the other, should be exerted during the ante-natal period. The most important factors contributing to a high rate of breast feeding were college education of the mothers and higher social class. Fashion plays a part in breast feeding and at present it is fashionable among the better educated to try to breast feed their infants. This is probably due to what they read about the value of a close mother-child relationship in magazine articles about psychiatry. The trend of decline in the lower social groups still persists as they are less exposed to psychiatric thought on the matter.

*Allen Daley*

DEAS, K. S. **Analyses of Intake of Welfare Foods by 5,193 Edinburgh Infants.** *Med. Officer.* 1958, Oct. 3, v. 100, No. 14, 223–6.

There were 7,005 children born in Edinburgh during the 12 months ended June 30, 1955 who survived 9 months. Information was obtained about 5,193 of them at the 3rd and 9th months.

*Vitamin C.* The percentages receiving supplements of this vitamin were 87 at the 3rd and 92 at the 9th month: 75% at the 3rd and 74·6% at the 9th month got it in the form of National Orange Juice but in only 42·7% and 24% was the dosage regarded as adequate. The alleged reasons for giving a proprietary preparation instead of the national issue (or none at all) were that the latter caused sickness or "spots" (32·2% at 3 months) or the child refused it (30·7%). In 26·7% the health visitor regarded the failure to give it as parental carelessness or negligence.

*Vitamin D.* At both ages 78% were receiving a vitamin D supplement and in 70% at age 3 and 67% at 9 months it was in the form of National Cod Liver Oil but in only 22·7% at 3 and 56·8% at 9 months was the amount regarded as adequate. The reasons for not giving it are set out in a table. At 3 months 39% of the children refused it: in 15·5% it caused alimentary disturbance and in 11·4% the mother disliked the taste or the smell. In 23·6% the health visitor regarded the failure to give it as due to the mother's carelessness. At 3 months 8·7% of the children and at 9 months 10·5% were getting a proprietary preparation of vitamin D but at both ages 20% had no supplement.

The main finding is that for both vitamins "the majority of Edinburgh infants were having welfare foods in their diets but that they were commonly having them in doses lower than those recommended".

On the other hand a "considerable number" who had additional sources of vitamin D from National Dried Milk "might well have had daily intakes above the level regarded by some as toxic". *Allen Daley*

ČESKOSLOV. HYG. Prague. 1959, v. 4, Nos. 2/3, 65–228, numerous figs. [Numerous refs.] English summaries. Školská hygiena. [**School Hygiene in Czechoslovakia**]

This issue of the journal comprises a record of a congress held in November 1958, and some of the papers deal with the history of school health services in various eastern European countries, and in France and Denmark. These papers are followed by others in which various hygienic problems of school life are discussed, and which range from blood studies to studies of the daily regimen of the pupils, and of the effect of school life on their psychological and nervous development.

The papers include short summaries in English.

*Charles Wilcocks*

COHEN, G. J. & AHRENS, W. E. **Chronic Lead Poisoning. A Review of Seven Years' Experience at the Children's Hospital, District of Columbia.** *J. Pediatrics.* St. Louis. 1959, Mar., v. 54, No. 3, 271–84, 4 figs. [35 refs.]

In the 7-year period 1950–6 a total of 43 infants and children were admitted to the Children's Hospital, District of Columbia, for chronic lead poisoning. It is the purpose of this article to review this experience in detail and in the light of previous reports and modern opinion.

"Lead poisoning is still a significant cause of mortality and morbidity in children" and reports indicate that its incidence is much higher in the United States than in Britain. The most important cause of lead poisoning in children is the ingestion of lead-containing substances of which the most widely reported are paint from walls and woodwork and plaster [this *Bulletin*, 1953, v. 28, 33, 83; 1955, v. 30, 658, 734; 1956, v. 31, 236; 1957, v. 32, 302]. In the experience of these 43 patients evidence of the pica habit was obtained in 40 of the children.

There is description and discussion of published reports on the psychological background of the pica habit, the age distribution of the children and the higher incidence of lead poisoning in the summer months. "There seems to be little correlation between the incidence of lead poisoning and sex or race of the patient." The symptoms, pathological changes, X-ray findings, results of laboratory tests, treatment with EDTA and prognosis as recorded in the literature are described. A detailed analysis of the data obtained from the 43 children was made and is described with numerical tables and X-ray photographs to illustrate bony changes in lead poisoning.

"Chronic lead poisoning has become an increasingly significant problem as awareness of the diagnosis, treatment, and residuals has increased." In this series of cases the mortality was high (7%) but even more important was the "45 per cent incidence of neurologic and psychiatric residual morbidity."

Methods which should be adopted for the prevention of lead poisoning in children are outlined with mention of the establishment at the authors' hospital of a Lead Poisoning Clinic for the purpose of screening all pica cases, standardizing in-patient therapy, providing better follow-up of discharged patients and offering psychiatric assistance. *M. E. Delafield*

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# Health of Nurses, Students and Hospital Staffs

QUEEN'S UNIVERSITY OF BELFAST. **Student Health Committee. Report of Medical Officer** [JOHNSTON, W.]. Tenth Annual Report. Academic Year 1957–58. 8 mimeographed pp. + 22 pp. of tables. [1959.]

Part I of this the 10th Annual Report on the Student Health Service of the Queen's University of Belfast gives a general survey of the year's work and compares the numerical data of consultations, treatments and other medical action in the academic year 1957–8 with those of 1948–9. The volume of work done has increased very greatly since the inception of the Student Health Service.

In the year 1957–8 the general health of the student population was good and though influenza morbidity was high all those infected recovered completely. Preventive inoculation against poliomyelitis and against tetanus was offered and the response was good. An interesting experiment was made of giving vitamin E to a selected group of athletes as the success of Australian athletes at the Melbourne Olympic Games had been attributed in large measure to this medication. The conviction which was reached, though not proved, was that vitamin E "had a considerable effect in delaying muscle fatigue and thus increasing stamina and muscle endurance without any side-effects whatever".

Casual consultations increased greatly in number—4,376 students and 601 staff. Routine medical examinations were carried out on 697 freshers. Examination of the 82 medical students who were about to begin clinical work showed that 32 of these were Mantoux negative. BCG vaccination was done on 31 and 1 was to be done at a later date. Treatment was provided for 3,945 students and staff. Part II of the report deals with tuberculosis and the findings of mass miniature radiography. 1957–8 is the first year in which no active cases have been found either in the 697 freshers or the 2,634, senior undergraduates. All the students who had been reported in previous years and were under treatment have now recovered. Continued vigilance is needed for in 1958–9 active disease has again been discovered in 2 freshers and 1 second year student.

In the Appendix there are many pages of statistical data derived from the year's work.

[For 9th Annual Report, see this *Bulletin*, 1958, v. 33, 631.] *M. E. Delafield*

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# Vital Statistics and Epidemiology

REGISTRAR GENERAL, ENGLAND & WALES. **The Registrar General's Statistical Review of England and Wales for the Year 1956. Part III. Commentary.** pp. xvi + 294, illustrated. 1958. London: H.M. Stationery Office. [16s. 6d.]

Among the special features of the *Medical Tables* and *Civil Tables* discussed in this *Commentary*, a comparison of national infant mortality rates shows that in Europe only Sweden and the Netherlands had lower rates than the England and Wales figure of 23·7 per 1,000 live births. The continued decline in England and Wales in the previous 5 years affected mainly gastro-enteritis, pneumonia and bronchitis and the infectious diseases, while mortality from congenital malformations, postnatal asphyxia and birth injuries changed little.

Continuing the rapid decline in recent years, the crude death-rates for all forms of tuberculosis in 1956 had fallen 16% for males and 20% for females below those in 1955. All age-groups below 65 years shared in this fall, but above this age there was little or no change. Over 90% of male deaths and just under 90% of female deaths were due to respiratory disease. For this form maximum mortality in males in 1946 was in the age-group 55–64 years, with a rate of 1,165 per million; in 1956 the maximum occurred later, at ages 65–74 years but with a much lower rate of 640 per million. For women the change was more striking, as maximum mortality in 1946 was 842 per million at ages 20–24, compared with 125 per million at age 75 and over in 1956. In contrast with mortality, notification rates after the war increased, probably as a result of improved diagnosis and case-reporting, but by 1956 the downward trend at all ages except those over 65 years suggested a real decrease in incidence.

For non-respiratory tuberculosis the decline in death and notification rates has been more impressive, particularly so for disease of the meninges and central nervous system. Whereas mortality from respiratory tuberculosis in 1956 was about 20% of that in 1946, from tuberculosis of the meninges and central nervous system it was only 5% of that 10 years earlier.

Geographical comparisons showed that for respiratory tuberculosis the Eastern region had the most favourable mortality and notification rates, about two-thirds of the average for the whole country. London and the South Eastern region had low mortality but high notification rates, suggesting an efficient case-finding service, while Wales, Midland, Northern and North Western regions had both high mortality and notification rates, the Tyneside and Merseyside conurbations being particularly prominent.

The Mass Miniature Radiography Units made over 3½ million examinations in 1956 and found 7,240 cases, a rate of 2·0 per 1,000 examinations, compared with 2·2 in 1955. This fall in the diagnosis rate affected all age-groups and both sexes. The highest incidence was found among patients referred by general practitioners, 11·9 per 1,000 for males and 7·2 for females. General public volunteers and persons in factories and offices together produced over one-half the cases diagnosed by the units in 1956, but the rates, about 2 per 1,000 examinations, were among the lowest of any groups.

In 1956 cancer was recorded as the cause of death of 48,935 men and 43,775 women. Cancer of the lung accounted for 32% of these deaths in men but for only 6% in women. Whereas mortality for this site continued to increase, that for cancer of the digestive tract fell, although in both sexes it was still responsible for about 40% of all cancer deaths.

A detailed commentary is provided on mortality from leukemia which has increased steadily during this century. The characteristic age pattern was bimodal with a peak about the fourth year of life and a second rise commencing about the thirtieth year to reach a peak in the 75–79 age-group. This pattern was repeated in each of the 4 quinquennia 1921–5, 1931–5, 1941–5 and 1951–5, except that each successive curve was set higher than its predecessor. Lymphatic leukemia was the most common type in childhood, accounting for nearly one-half of all leukemia deaths under 15 years. After childhood, mortality from this type fell and that from myeloid was commoner in middle life, while in old age each accounted for approximately the same proportion. Monocytic and acute unspecified forms were less common as a cause of death at all ages. There was no evidence that the death-rate from any one of these types was increasing faster than the rest. Death-rates from leukemia were in general highest in the southern part of England and Wales, but geographical comparisons did not show a regular association between excess mortality from leukemia as a whole and an increase in either myeloid or lymphatic forms. The most common form of leukemia occurring after excessive exposure to artificial radiation is of the myeloid variety. These secular trends and regional variations in leukemia mortality do not accord, therefore, with the suggestion that they may be largely due to an increase in exposure to radiation.

In other sections of the *Commentary* details are listed of the 3 deaths assigned to complications of smallpox vaccination and of the 5 deaths assigned to other complications of prophylactic inoculations, 3 of them associated with anti-tetanus serum. Deaths of 22 males and of 15 females were assigned to tetanus itself, and in a further 11 males and 4 females it was mentioned although the death was assigned to other causes.

An account is given of an investigation carried out by the General Register Office in 1955 on data provided by 10 hospitals performing post-mortem examinations as a routine. A comparison was made between the cause of death assessed by a clinician before post-mortem examination with that given by a pathologist afterwards. On the basis of the International Statistical Classification there was agreement in 51% and disagreement in 49% of cases. There was disagreement of fact in 19%, in matters of interpretation and wording in 28%, and in 2% the pathologists' certificates were incorrect. With increasing age of the patients disagreements of fact and opinion became commoner. Degenerative diseases and in particular arteriosclerotic heart disease were difficult to classify and some diseases, notably cancer of the lung, were probably under-diagnosed by clinicians. Despite the differences in nearly one-half the cases, the net effect is thought to be small.

*J. Knowelden*

# Communicable Diseases

*For the bacteriology of these diseases see the section on Bacteriology below. For those communicable diseases conventionally regarded as tropical, readers are referred to the* TROPICAL DISEASES BULLETIN

## INFECTIVE DISEASES

*In this section the abstracts are arranged as far as possible in the following order:—General; Diphtheria, Whooping Cough, Streptococcal Infections, Staphylococcal Infections, Measles, Mumps; Chickenpox, Smallpox; Influenza and other Respiratory Virus Infections, Pneumonia; Hepatitis, Mononucleosis; Meningitis, Poliomyelitis and other Enteric Virus Infections; Encephalitis; Enteric Fevers.*

AKYAY, N. Türkiyede difteri problemi ve kitle immünizasyonu ile eradikasyon imkânlari. [**Diphtheria in Turkey and Possibilities of its Eradication by Mass Immunization**] *Türk Ijiyen ve Tecrübî Biyoloji Dergisi.* Ankara. 1958, v. 18, Nos. 2/3, 168–81, 1 graph. [14 refs.]

The English summary appended to the paper is as follows:—

"Diphtheria in Turkey has increased greatly in the recent years and its rate of morbidity has reached to the same level of typhoid fever, measles and whooping-cough. In 1957, the rates per 100,000 were for typhoid fever 21.4, for whooping-cough 20, for measles 82 and for diphtheria 20.1."

SUTIN, I. A., BENDERSKAIA, E. A., POLIAKOVA, I. L., NAIMAN, Z. I., EPSHTEIN, R. V. & FOGEL'SON, T. A. **The Epidemiology of Diphtheria of Dietary Origin.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 9, 1410–14. [Translated from Russian.]

In town S., apparently near Stalingrad, in the first 4 months of 1957, 74 cases of diphtheria occurred: in only 6 instances were the patients over 15 years old. In the first 10 days of May, 192 persons contracted the disease: 45% were adults and 36% older children, so that quite a different age-group was affected. Infection appeared to have taken place either during May Day demonstrations on May 1 or at a mass picnic on May 2. The common article of diet appeared to be ice-cream. Of the ice-cream factory workers, one had been discharged from hospital after diphtheria on April 13, one was in contact with a diphtheria patient on April 20, and one became ill on April 28 and was subsequently diagnosed as suffering from diphtheria. Of 5 workers who made the ice-cream one developed diphtheria after May 1 and one proved to be a carrier. 4 other factory workers contracted diphtheria and 2 more were proved carriers. The ice-cream was prepared by hand and samples were taken by sucking it up through a tube by the mouth. The milk was pasteurized but the mixture was not and was left for 15–17 hours before freezing. No ice-cream was available for bacteriological examination. The strain isolated from the patients proved to be of *mitis* type and non-toxigenic. No clinical details are given except that the disease was localized in the pharynx and tonsils and that there was no toxaemia but some pyrexia.

*A. B. Christie*

FAERMAN, N. N. **Treatment of the Carrier State in Diphtheria with Chlortetracycline.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 9, 1390–93. [13 refs.] [Translated from Russian.]

Chlortetracycline in doses varying between 12,500 and 100,000 units 4 times a day for 3 to 7 days was given to 88 diphtheria carriers. The organism in the great majority disappeared after 2–3 days of treatment. In 4 patients, the drug proved ineffective though 3 of the children eventually had negative swabs. Treatment with chlortetracycline in addition to diphtheria antitoxin in the acute stage of the illness reduced the convalescent carrier rate by 3·5 times. The definition of the carrier state seems different from that used in Britain: in 65% the organism could be isolated for a period not exceeding 2 weeks and in only 3% did the state last over 1 month. [It appears in fact that what is in question is the effect of the drug on the period of infectivity after an attack of the disease rather than its effect in clearing the organism from chronic carriers.]

*A. B. Christie*

D'ALÒ, G. La vaccinazione "di richiamo" con anatossina fluida nella profilassi antidifterica d'urgenza. [**Reinforcing Vaccination with Fluid Anatoxin in Urgent Antidiphtherial Prophylaxis**] *Igiene Moderna.* 1958, Sept.–Oct., v. 51, Nos. 9/10, 651–9. [41 refs.] English summary.

Attention is drawn to the possibility of fatal diphtheria infection in closed communities of immunized children for some of whom the previous inoculation may have been remote. The very rapid response of such individuals to fluid anatoxin, 100% Schick conversion within 8–10 days, with absence of anything more than trivial reaction to the injection, led the author to consider this the best measure available, especially since it eliminates the use of antiserum and the severe allergic reactions to which it may give rise.

*J. W. McLeod*

KNOTHE, H. & LAFORET, W. Zur Frage der seuchenhygienischen Massnahmen bei Diphtherie-Bakterienausscheidern. [**On the Hygienic Regulations for the Control of Carriers of the Diphtheria Bacillus**] *Öffentl. Gesundheitsdienst.* Stuttgart. 1958, v. 20, No. 9, 346–53.

The regulations for the control of diphtheria carriers in Germany are carefully reviewed and attention is drawn to a number of weaknesses and inconsistencies in these regulations, as *e.g.* the absence of any specific attempt to check the participation of diphtheria carriers in the distribution of food products.

The authors record that among 63 carriers of the diphtheria bacillus from whom isolations were made in 1956, 19 *gravis*, 44 *mitis* and no *intermedius* strains were isolated. Toxicity was determined by tests on guineapigs, on the embryo chicken and by agar diffusion methods. 12 *gravis* and 3 *mitis* were found to be toxic and 7 *gravis* and 41 *mitis* strains were found to be non-toxic. The suggestion that carriers of *mitis* strains which are non-toxic by laboratory tests do not require further control is discussed. *J. W. McLeod*

FRYKHOLM, R. Nosocomial staphylococcinfektion på en neurokirurgisk avdelning. [**Nosocomial Staphylococcal Infections in a Neurosurgical Ward**] *Opuscula Med.* Stockholm. 1958, Oct., v. 3, No. 8, 283–6. English summary (6 lines).

In 1957 an outbreak of infections due to *Staphylococcus aureus* occurred in a neurosurgical ward in a Stockholm hospital. The organism could be recovered from most of the patients and the staff, and the infection could only be overcome by evacuating the ward and subjecting it to thorough cleaning and disinfection. The infection took a serious course in 5 patients who had undergone craniotomy, and in 2 was the direct cause of death. The histories of 7 cases are given in illustration. *D. J. Bauer*

POLLARD, B. R. & PERRY, S. E. **Haemolytic Streptococci in a Maternity Unit.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council.)* 1959, Mar., v. 18, 46–8.

It was decided to investigate the distribution of group A streptococci in a 12-bedded maternity hospital after a case of puerpral sepsis in November 1957 and the death of an infant in January 1958 due to this organism.

Type 28 group A streptococci were found in umbilical swabs from 8 out of 12 infants, the throats of 1 mother and a night-sister. Later one day-sister and the night-sister who delivered the woman who developed puerpral fever were also found to be carriers of the organism, which was widely distributed throughout the maternity hospital but absent from the labour ward.

Haemolytic streptococci were eradicated by fumigation of the building with a fog generator with 10% formaldehyde solution. The operation took 5 minutes for a room and rooms were ready for reoccupation in 6 hours. *M. Patricia Jevons*

PHILIP, R. N., REINHARD, K. R. & LACKMAN, D. B. **Observations on a Mumps Epidemic in a "Virgin" Population.** *Amer. J. Hyg.* 1959, Mar., v. 69, No. 2, 91–111, 5 figs. [44 refs.]

In 1957 an epidemic of mumps occurred among the Eskimos who inhibit St. Lawrence Island which is situated in the Bering Sea 120 miles from Alaska. It is probable that mumps had not occurred previously on the island within the lifetime of present residents. The population of 561 Eskimos live in 2 villages of approximately equal size. The infection was probably introduced by a boy who developed bilateral parotitis in December, 1956 a few days after his return from a hospital in Fairbanks, Alaska where mumps was occurring sporadically. In January 1957 2 members of his family developed mumps. The epidemic at first spread slowly but then gathered force and reached a peak in late April in 1 village and about 1 month later in the other village after which it subsided rapidly.

The paper contains an interesting and detailed account of the island and of the extensive epidemiological, clinical and serological observations which were made. The method used for measuring the complement-fixation antibody titre is described. In 1955 the sera of 129 persons in the island had been examined and after the epidemic 333 (59%) and 216 (38%) of the total population of 561 were tested in July 1957 and February 1958 respectively. The epidemiological and serological data are set out in a number of tables and charts.

In summary 65% of all the Eskimos had clinical mumps, but on the basis of clinical history and post-epidemic serological results the total of infections was 88%. Frequency of attack was similar in the 2 villages and was highest in school-age children and young adults. "Only 3 per cent of persons had demonstrable antibody prior to the epidemic but 85 per cent had demonstrable antibody after the epidemic." Of the total of 363 cases 205 were in males of whom 52 (25%) had orchitis. It appeared that pregnant women were less prone to infection and probably to clinical mumps than non-pregnant women. *M. E. Delafield*

ORTEL, S. Ergebnisse und Erfahrungen mit der Mumps-Komplementbindungsreaktion. [**Results and Experiences with the Mumps Complement-Fixation Test**] *Ztschr. f. ärztl. Fortbildung.* 1958, Nov. 15, v. 52, No. 22, 944–6, 1 fig.

Mumps complement-fixing antibody was found in titres of 10 to 640 in 114 of 233 sera and 5 of 22 cerebrospinal fluids from 155 children treated in hospital between 1955 and 1958 with a diagnosis of mumps, meningitis, encephalitis or pyrexia of unknown origin. A titre of 160 or higher, indicative of a recent infection, was found in 55% of instances. In the patients suffering from clinically evident mumps the titre usually reached diagnostic levels in the 3rd week of illness; 55% of the patients with mumps antibody were aged 6–10 years, and 38% were aged up to 5 years. In an examination of 82 sera from persons not suffering from mumps 48 were found to have titres not exceeding 10. *D. J. Bauer*

SZATHMÁRY, J. & HOLIK, S. **The Specificity of the Vaccinia Haemagglutination-Inhibition by the Cerebrospinal Fluid.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 4, 329–35, 1 fig. [14 refs.]

"Normal cerebrospinal fluid is unable to exert an effect upon vaccinia haemagglutination. Cerebrospinal fluids containing a pathologically high amount of protein exhibit haemagglutination inhibition, independently of whether they originate from patients who have been vaccinated a few months or many years earlier, or from unvaccinated children in the 3-month to 5½-year age group. No relationship exists between the inhibition titre of the serum and the inhibition observed in the cerebrospinal fluid. It is the globulin fraction that possesses the property of inhibiting haemagglutination. It is assumed that the haemagglutination inhibition observed in some cases was wholly or partly due to the action of non-specific substances."

ALIVISATOS, G. P. & VIOLAKI-PARASKEVA, M. Die Virämiedauer nach Vakzination und Variolaerkrankung. [**The Duration of Viraemia after Vaccination and Smallpox**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Mar., v. 117, No. 3, 230–43, 5 figs. [14 refs.]

Blood samples were taken from 24 infants 35–73 days after successful primary vaccination. The blood was stored at −22°C. in 60% glycerol until it was inoculated to the chorio-allantoic membranes of 4–6 12-day chick embryos. The membranes were examined for the presence of pocks after 2 days' incubation. 15 of 24 infants had a viraemia according to the published results.

The authors also report the presence of circulating variola virus in a man 38 days after the onset of smallpox and 14 days after the crusts had come off his lesions. [The slightly enlarged photograph of a chorio-allantoic membrane published in support of this claim shows a fairly well developed non-specific lesion and several white spots, most of them about 1 mm. in diameter (allowing for an enlargement of the photograph of not more than 2 × ).] *Colin Kaplan*

BULL. WORLD HEALTH ORGANIZATION. Geneva. 1959, v. 20, Nos. 2/3, 183–508, numerous figs. [Numerous refs.] **Influenza.**

A series of reports dealing with many aspects of influenza are brought together in this publication. Studies carried out during the 1957 Asian influenza pandemic are presented by workers from several countries (FUKUMI, H., *Summary report on the Asian influenza epidemic in Japan, 1957*, pp. 187–98; MENON, I. G. K., *The 1957 pandemic of influenza in India*, pp. 199–224; PRZESMYCKI, F., SAWICKI, L., DOBROWOLSKA, H., GRZELAKOWA, A., ZANSKI, J., STASIK, M., KULESZA, S., ZGORZELSKA, K. & CIEPLINSKA, Ś., *The epidemic of Asian influenza in Poland, 1957*, pp. 225–39; BERKE, Z., *The Asian influenza pandemic in Turkey, 1957–58*, pp. 494–8; PACCAUD, M. F. & PONCIONI, B., *La pandemic grippale de 1957 et les autres maladies respiratoires à virus dans le canton de Genève* (Suisse), pp. 498–504). These reports include data on the epidemic spread, morbidity and mortality rates, clinical features, laboratory investigations and preventive and therapeutic measures used in each country.

The incidence of influenza in French Equatorial Africa is discussed by R. DEPOUX, J. ORIO, C. CHIPPAUX, & P. MERVEILLE, (*La grippe dans la population africaine de Brazzaville*, pp. 241–50). Complement-fixation and haemagglutination inhibition tests performed in sera of 368 African subjects living in Brazzaville gave evidence of relatively frequent infections by influenza A and B. Such infections have often remained undiagnosed, except in early 1958 when the disease was expected to occur.

Investigations carried out in the U.S.S.R. between 1954 and 1958 and especially during the 1957/8 epidemic are presented in 3 articles (JDANOV, V. M. & RITOVA, V. V., *Quelques particularités cliniques et sérologiques de la grippe en 1957/58 chez des enfants*, pp. 251–9; ZHDANOV, V. M., *Results of further research on influenza in the U.S.S.R. with special reference to the 1957 pandemic*, pp. 261–96; ZHDANOV, V. M., *The 1957 influenza pandemic in the U.S.S.R.*, pp. 489–94). The occurrence of influenza A, B and C and of para-influenza (influenza D) in the U.S.S.R. is reported. Asian strains (referred to in most of the articles in this volume as influenza A2) isolated during the 1957–8 epidemic were divided into 2 groups consisting of avid and non-avid strains respectively. The biological distinction between these 2 groups is presented and discussed. The pathogenesis and immunology of influenza is considered. The disease is often biphasic, the first phase consisting mainly of upper respiratory symptoms followed, in the case of non-immune individuals, by a second phase of pulmonary involvement. It is suggested that the virus spreads to the lungs *via* the blood stream and that this may be prevented by intramuscular injections of hyperimmune anti-influenza serum. Clinical observations, epidemiology and diagnosis of Asian influenza are discussed at some length. Treatment by antibiotics (penicillin, chlortetracycline and oxytetracycline) and chemotherapeutic substances (meparine and Kutizon—a thiosemicarbazone derivative) had no effect on the primary virus infection. The therapeutic use of hyperimmune anti-influenza serum is reported as highly effective in reducing the duration of illness and the number of complications (no detailed figures given). The influenza mortality during the 1957–8 pandemic is said to have been lower in the U.S.S.R. than in the U.S.A. and in England and Wales (no comparative figures or detailed criteria for assessing mortality rates are given) and Zhdanov believes that "the relatively low mortality figures in the USSR are a direct result of the system of State health services and free medical treatment of the public, and are also based on the large amount of work carried out by the medical profession everywhere before and during the pandemic". Field trials designed to assess the efficacy of a live Asian virus vaccine administered by the respiratory route gave encouraging results and minimal requirements for vaccine production are proposed. Evidence suggesting that infection by an A-prime virus may be followed by a short period of resistance to the Asian strain is presented by A. N. SLEPUSHKIN (*The effect of a previous attack of A1 influenza on susceptibility to A2 virus during the 1957 outbreak,* pp. 297–301).

Epidemiological and laboratory studies conducted in Poland between 1947 and 1957 are presented (Przesmycki, F., Dobrowolska, H. & Sawicki, L., *Epidemiology of influenza in Poland, 1947–57,* pp. 303–23) suggesting that influenza epidemics are either "imported" or originate from virus pre-seeded in the population. Isolation of a strain resembling PR8 in 1953 and thought not to have arisen from laboratory contamination is reported.

Work carried out between 1956 and 1958 in Czechoslovakia is presented (RĂSKA, K., TUMOVÁ, B., PECENKA, J. & RADKOVSKÝ, J., *Report on the first two years of the Czechoslovak Influenza Centre,* pp. 325–32). Virus strains isolated in Czechoslovakia included types A-prime in early 1957, Asian, from May 1957 to June 1958 and B strains in early 1958. The last differed from previously isolated B strains, as shown by haemagglutination-inhibition tests. Morbidity and mortality rates observed during the 1957–8 epidemic are presented and preliminary results suggesting the effective use of hyperimmune horse serum for prophylaxis of influenza are reported.

Results of clinical trials demonstrating the efficacy of polyvalent formalin-inactivated vaccines administered by the intranasal route are presented by Polish workers (Przesmycki, F., Sawicki, L. & Dobrowolska, H., *Vaccination against influenza in Poland, 1953–56,* pp. 333–53). Advantages of intranasal over parenteral routes of vaccination are discussed and the inclusion of a large number of strains in the vaccine is recommended.

Experience on the use of inactivated virus vaccines administered by parenteral routes is presented by workers from several countries. H. Fukumi (*Human vaccination experiments with Asian influenza vaccine in Japan,* pp. 355–76) investigated the antigenicity of vaccines prepared with different Asian strains and recommends the use of monovalent vaccines prepared with P-phase strains and administered in 2 rather than single doses.

Studies on the antigenicity and protective effects of formolized monovalent Asian influenza vaccines are reported by L. HELLER, B. KORLOF, J. MÖRNER and B. ZETTERBERG (*Serological and prophylactic trials of Asian influenza vaccines in Sweden,* pp. 377–400). The relation between antibody-stimulating and protective effect of influenza vaccines was investigated in 2 clinical trials and methods of expressing vaccine potency are discussed.

Antibody responses and degree of protection conferred by 2 doses of a monovalent Asian influenza vaccine containing each 100 chicken cell agglutinating (CCA) units of formalin-inactivated virus adsorbed on aluminium phosphate are presented by J. SIGURJÓNSSON, B. SIGURDSSON and H. GRÍMSSON (*Experience with influenza vaccination in Iceland, 1957,* pp. 401–9).

Methods used for the identification of influenza virus types and strains by complement fixation are presented by F. S. LIEF and W. HENLE (*Methods and procedures for use of complement-fixation technique in type- and strain-specific diagnosis of influenza,* pp. 411–20). The preparation of type-specific S (soluble) and strain-specific V (virus) antigens and antisera and their use in complement-fixation tests are described in detail [see also Lief, Fabiyi & Henle, this *Bulletin,* 1958, v. 33, 709; Fabiyi, Lief & Henle, *J. Immunology,* 1958, v. 81, 467; Henle, Lief & Fabiyi, this *Bulletin,* 1958, v. 33, 710].

A study of variations in haemagglutination-inhibition of Asian influenza strains by normal and immune sera is presented by H. Fukumi (*Studies on the P–Q phases of A/Asia/57 influenza viruses,* pp. 421–34). Strains in P-phase were shown to stimulate better neutralizing antibody responses than those in the Q-phase. The implication of this finding on the selection of virus strains for vaccine production is discussed.

The relationships and main characteristics of human respiratory viruses are presented by C. H. ANDREWES and G. WORTHINGTON (*Some new or little-known respiratory viruses,* pp. 435–43). Myxoviruses are divided into 2 sub-groups, the first consisting of true influenza viruses (types A, B and C) and the second gathering together mumps, Newcastle disease and para-influenza viruses. Among the type A influenza viruses are included agents isolated from man, swine, horse, duck and fowls (fowl-plague virus). The para-influenza viruses are subdivided into para-influenza 1 (Sendai or influenza D, haemadsorption virus type 2), para-influenza 2 (croup-associated or laryngo-tracheobronchitis virus) and para-influenza 3 (haemadsorption virus type 1). The pathogenicity of some myxoviruses for mice and ferrets is reported. The role of Coxsackie, ECHO and other viruses in the aetiology of acute upper respiratory disease is discussed.

A comparative study of Asian and type A influenza viruses isolated from horses in Czechoslovakia is reported by B. TUMOVÁ and O. FISÉROVÁ-SOVINOVÁ (*Properties of influenza viruses A/Asia/57 and A-equi/Praha/56. 1. Agglutination of red blood cells,* pp. 445–54). Asian and horse strains can be distinguished from other myxoviruses (type A, A-prime, B, C, Sendai, mumps and Newcastle disease viruses) by their ability to agglutinate swine, calf and horse erythrocytes.

Experimental infection of pigs with the Asian influenza virus is reported by G. D. WALLACE and R. E. KISSLING (*Studies in swine of Asian influenza virus,* pp. 455–63). Evidence of infection was obtained on the basis of virus isolations and antibody responses. No evidence was obtained to suggest that pigs played a significant role in the epidemiology of Asian influenza in the U.S.A. or that the Asian virus established itself in swine. The capacity of Asian influenza virus to cause natural inapparent infection in horses and swine is, however, suggested by M. M. KAPLAN and A. M.-M. PAYNE (*Serological survey in animals for type A influenza in relation to the 1957 pandemic,* pp. 465–88). A world-wide survey of influenza antibodies in animal sera showed, in addition, that horse influenza caused by A-equi strain is present in many countries and that infection of pigs by A-swine strain occurs in some European countries.

*H. G. Pereira*

Blair, W., Brown, W. K., Caldwell, W. F., Clarke, A., Dunn, S., Primrose, D., Stewart, T. F., Grist, N. R. & Sommerville, R. G. **Influenza Studies in General Practice in the Glasgow Area.** [Memoranda.] *Brit. Med. J.* 1959, Feb. 14, 422.

A team of general practitioners, working in association with a virological laboratory in the Glasgow area, are carrying out a series of investigations on influenza-like illnesses. Serological tests in 252 patients during the period of the Asian influenza epidemic in 1957, and its recrudescence in the spring of 1958, showed rising titres to type A infection, with 78% positive in Sept.–Oct. 1957, and 45% positive in Jan.–Feb. 1958. No cases of type B or C influenza infection were detected. 4 patients showed at least 4-fold increases in complement-fixing antibody to adenovirus particularly types 2 and 7. Among 37 patients with proved type A influenza and 45 with negative laboratory findings, the clinical features, headache, sweating, muscle pain, cough, pharyngitis, nasal congestion and discharge, showed an almost equal incidence in the two groups. [It is clear that in influenza-like illnesses an aetiological diagnosis cannot be made from clinical signs alone.]

[For earlier studies see this *Bulletin*, 1957, v. 32, 405.]

*H. Stanley Banks*

McWilliam, Joan M., with the technical assistance of Agnes P. H. Anderson. **Antibodies to Asian Influenza and Influenza B: Edinburgh, 1958.** *Brit. Med. J.* 1959, Feb. 21, 473–6, 4 figs. [11 refs.]

In the post-epidemic period (August and September 1958) a study was made of antibodies to influenza Asian type A and to type B (Lee), in the serum of a cross section of the adult population in Edinburgh. The sera were collected mainly from blood donors, but some were obtained from the City Hospital, from general practitioners, and from patients with bronchitis. Among 1,187 sera examined 413 (34·8%) showed antibodies to type A, and 1,076 (91%) to type B. The antibody titre to Asian influenza was highest in the 11–15-year age-group and almost at its lowest in the 25–40-year age-group. By contrast, the antibodies to influenza virus B were very low in children and rose to a high plateau throughout the adult age-groups.

A practical deduction from this study would seem to be that vaccination against Asian influenza of adults aged 25–40 in key positions in the community, would be rewarding both economically and otherwise. Since many would already have a low basal immunity, a single boosting dose might be protective.

*H. Stanley Banks*

Vojtová, Helena. Chřipka v Jihlavském kraji v zimě 1957. [**Influenza in the Region of Jihlava in Winter 1957**] *Českoslov. Epidemiol., Mikrobiol., Imunol.* Prague. 1958, v. 7, No. 6, 374–9, 1 graph. [16 refs.] English summary (6 lines).

In January 1957 an outbreak of influenza occurred in a children's home in Jihlava, Czechoslovakia, and also in other communities in the town. 3 strains of virus were isolated from nasal washings and were identified as A-prime, and of 27 paired sera taken from patients during the acute and convalescent stages of the disease 15 showed a diagnostic 4-fold or greater rise of titre in haemagglutination-inhibition tests and 19 were similarly positive in complement-fixation tests. Towards the end of February a second outbreak of influenza occurred in the children's home, and also in a student's hostel in the town; 6 strains of influenza virus were isolated and found to be of type B. *D. J. Bauer*

Mark, D. D. **The Pathology of 1957 (Asian) Influenza.** *Amer. Rev. Tuberculosis.* 1959, Apr., v. 79, No. 4, 440–49, 12 figs. [16 refs.]

"The pulmonary pathology has been described in seventeen fatalities associated with the 1957 influenza epidemic. Evidence of influenzal infection was established in 6 patients by viral isolation from the lung, and in 4 patients by antibody studies. The lungs of all of the patients showed a characteristic necrotizing tracheobronchitis with foci of squamous metaplasia in the mucosa which is considered a distinctive feature of influenzal viral infection. Two patients exhibited isolated tracheobronchitis without a complicating pneumonia.

"The importance of *Staphylococcus aureus* as a predominant superinfecting organism in fatal cases is indicated."

Galloway, R. W. & Miller, R. S. **Lung Changes in the Recent Influenza Epidemic.** *Brit. J. Radiol.* 1959, Jan., v. 32, No. 373, 28–31, 5 figs.

This is a radiological analysis of lung complications occurring in influenza. Of 193 patients with clinical signs of pneumonia, 112 had radiological changes. Bronchopneumonia was the commonest finding. Pleural effusion was present in 12% and lobar and segmental consolidation in 5%. Only 1 case of lung abscess was discovered. 4 cases of active pulmonary tuberculosis were diagnosed. *A. B. Christie*

De Baan, P. Longafwijkingen bij Aziatische influenza. [**Pulmonary Changes in Asian Influenza**] *Nederl. Tijdschr. v. Geneesk.* 1959, Apr. 4, v. 103, No. 14, 721–6, 7 figs. [28 refs.]

The English summary appended to the paper is as follows:—

"A description is given of the pulmonary changes in 10 patients who died of Asian influenza in the period October 1957–March 1958. The peculiar character of these changes warrants the conclusion that the virus had invaded not only the bronchial epithelium, but also that of terminal and respiratory bronchioles and of the most peripheral alveoli.

"The changes may be summed up as degeneration, necrosis and desquamation of the epithelium, accompanied by a haemorrhagic and fibrinous effusion in the lungs, and followed by vigorous regeneration of the epithelium at all levels mentioned.

"It is concluded that the Asian influenza virus has thus demonstrated pneumotropic properties in some cases."

Beswick, I. P. & Finlayson, R. **A Renal Lesion in Association with Influenza.** *J. Clin. Path.* 1959, May, v. 12, No. 3, 280–85, 2 figs. [19 refs.]

"Renal changes in seven fatal cases of influenzal pneumonia, due to virus A (Asian strain), are reported. The morbid anatomy and histology of the renal lesions, which were principally localized to the medullae of the organs, are described and illustrated.

"The literature on renal pathology in influenza is briefly reviewed; in several previous reports only cortical changes are described. It has not been possible to form a decided opinion as to the aetiology of the medullary lesions."

Herzog, H., Staub, H. & Richterich, R. **Gas-Analytical Studies in Severe Pneumonia. Observations during 1957 Influenza Epidemic.** *Lancet.* 1959, Mar. 21, 593–7, 2 figs. [22 refs.]

Of 125 patients suffering from Asian influenza in a hospital in Basle, 22 were dangerously ill and 12 died. Bacteriological findings showed the importance of staphylococci, and post-mortem examinations revealed the usual pulmonary features of extensive alveolar and interstitial haemorrhages and purulent inflammation. Gas analyses were carried out in the 22 dangerously ill patients. Hypoxia was present in all patients and there was a close connexion between the level of hypoxia and survival, but hypoxia was considered to be the main cause of death in only 1 patient. Irreversible cardiovascular collapse, seen in 8 patients, was the main cause of death. In many cases an arterio-alveolar $p\text{CO}_2$ gradient was observed, a sign of uneven alveolar perfusion. Tracheotomy with bronchial suctions could lead to a rapid rise in arterial oxygen saturation and aerosol isopropylnoradrenaline to a fall in $p\text{CO}_2$ where there was evidence of bronchospasm. Where oxygen unsaturation persisted after tracheotomy, artificial respiration by the Engström apparatus might then raise it. The effect of all these measures was not dramatic as regards survival figures—only 3 of 12 tracheotomized patients survived—but the authors feel that more energetic measures and more detailed study of these desperate cases should lead to improved results.

*A. B. Christie*

McEwan, T. **Dilacol in the Common Cold.** *Scottish Med. J.* Glasgow. 1959, Apr., v. 4, No. 4, 199–202.

"In the past 2 years a trial, in part controlled, has been carried out with a drug, proprietarily termed Dilacol, which appears to alleviate the symptoms" of the common cold. The patients were nurses in a city hospital. The drug is prescribed as a tablet which contains perdilatal (an organic chemical substance which is widely used as a peripheral vasodilator) 1·6 mgm., propyl salicylamide 60 mgm. and quinine hydrochloride 50 mgm. In the first 50 cases of colds the patients were treated alternately with the drug tablets and control tablets in a dosage of 2 tablets thrice daily for 2 days and then 1 tablet thrice daily for 3 days. Tables set out the results of the patients' experience in respect of 9 itemized symptoms over a period of 4 days. The general result was that 76% of the Dilacol group and 8% of the control group were cleared of the cold. In 2 nurses who were taking the drug some evidence of idiosyncrasy was manifested by palpitations or vertigo and tinnitus. In a further experiment with increased dosage of Dilacol the disappearance of symptoms of a cold was even more marked but about 20% of the nurses suffered from headache and there were other manifestations of toxic effects of the drug. Ultimately an intermediate dosage was decided on as the best to employ. There is an account of the significant differences found between the control and treated groups in respect of the separate symptoms of the infection.

The value of the drug lies not only in reducing the severity of the symptoms but also in producing a feeling of well-being throughout the illness. Nevertheless, longer trials should be instituted elsewhere to assess the effects of the drug more readily. *M. E. Delafield*

Fraser, P. K. & Hatch, L. A. **Outbreak of Adenovirus Infection in the Portsmouth Naval Command, 1958.** *Brit. Med. J.* 1959, Feb. 21, 470–73, 2 figs. [15 refs.]

The influenza A (Asian) epidemic of 1957 ended in the Portsmouth Naval Command in February 1958, and it was immediately followed by an explosive and widespread outbreak of adenovirus infection with the peak in February and March. Although this outbreak appeared to have arisen *de novo*, adenovirus infection was present in latent form in the Command in 1957, as shown by a 4-fold or greater rise in titre in 5 out of 767 paired sera tested in that year.

The chief symptoms were febrile sore throat with cough. Of 525 patients whose paired sera were tested, 201 showed 4-fold or greater rises in titre; further evidence of recent adenovirus infection was found in 210 of 373 patients from whom a single specimen of serum showed adenovirus titres of 1 in 20 or greater. Only 4 virus isolations were made from throat swabs or faeces of patients during the outbreak, all of adenovirus type 3.

During this investigation 4 out of 12 cases of pneumonia admitted to the general medical wards were proved to be advenovirus infections.

*H. Stanley Banks*

Chanock, R. M., Vargosko, A., Luckey, Alia, Cook, M. Katherine, Kapikian, A. Z., Reichelderfer, T. & Parrott, R. H. **Association of Hemadsorption Viruses with Respiratory Illness in Childhood.** *J. Amer. Med. Ass.* 1959, Feb. 7, v. 169, No. 6, 548–53.

The importance of haemadsorption viruses [Chanock *et al.*, this *Bulletin*, 1958, v. 33, 621] in the aetiology of acute respiratory infections was studied by clinical and laboratory methods. The study involved 1,738 children attending 3 hospitals in Washington D.C. Evidence of infection by haemadsorption virus types 1 and 2 among 879 children with respiratory illness was investigated by virus isolation and serological methods and the results were compared with those obtained among 859 children suffering from illnesses other than respiratory. Haemadsorption virus types 1 and 2 were isolated from 54 (6·2%) of the patients with respiratory illness and from 2 of the control patients. A higher incidence of infection by haemadsorption viruses was obtained by the complement-fixation technique. Both viruses were associated with a variety of clinical syndromes including pneumonia, croup, bronchiolitis, pharyngitis and febrile or afebrile mild respiratory disease. It was estimated that 19·5% of patients admitted to hospital with respiratory disease over the period from October 1957 to May 1958 showed evidence of infection by haemadsorption viruses.

*H. G. Pereira*

PARROTT, R. H., VARGOSKO, A., LUCKEY, Alia, HYUN WHA KIM, CUMMING, Christine & CHANOCK, R. **Clinical Features of Infection with Hemadsorption Viruses.** *New England J. of Med.* 1959, Apr. 9, v. 260, No. 15, 731–8, 2 figs.

2 new myxoviruses, haemadsorption types 1 and 2, first isolated in October 1957, are shown in this study of 92 patients to be associated with respiratory symptoms in children. The illness, whether due to type 1 or 2 virus, began with something resembling a common cold—pharyngitis, rhinitis, bronchitis and fever—and in 30 children the illness ceased after 3–4 days. In the others more severe respiratory illness, requiring hospital care, developed. There was a tendency for the 33 children in hospitals affected with type 1 virus to develop bronchopneumonia. The 29 affected with type 2 virus had a higher incidence of tracheitis and croup. Laboratory diagnosis of virus infection was by culture of oropharyngeal swabs and titration of complement-fixing antibody. [This is a detailed study, rather difficult to abstract adequately.] *A. B. Christie*

SAYMAN, W. A., GAULD, R. L., STAR, Shirley A. & ALLEN, J. G. **Safety of Liquid Plasma—a Statistical Appraisal.** *J. Amer. Med. Ass.* 1958, Nov. 29, v. 168, No. 13, 1735–9.

An investigation has been made of the incidence of hepatitis among patients given plasma or whole blood from the University of Chicago Blood Bank between 1942 and 1957. The plasma was obtained from blood which was unused after 5–6 days; it was combined in pools of material from 28–30 donors and was stored for about 6 months at a mean temperature of 31·6°C. (range 24·4–35·5°C.). A follow-up history covering the 6 months after transfusion was obtained in 433 of 442 (98·0%) patients given plasma only, in 1,242 of 1,263 (98·3%) given plasma and blood, and in 2,343 of 2,388 (98·1%) of a random sample comprising 21% of persons given blood only. 21 cases (3·2%) of serum hepatitis occurred among 653 patients given both blood and plasma, and 36 (1·9%) among those given blood alone. The authors point out that the reception of plasma from a large number of donors increases the chance of contracting hepatitis, and when allowance is made for this factor 48 cases of hepatitis would have been expected in the group given plasma only on the basis of the number due to the blood from which the plasma was made. In fact, no case occurred among 305 patients given plasma only, and the apparent safety of the material is attributed to the method of processing, which involved storage at a comparatively high temperature. *D. J. Bauer*

SOUSEK, O. Několik poznámek k otázce anikterického průběhu inf. hepatitidy. [**Some Comments on the Question of the Anicteric Course of Infective Hepatitis**] *Časopis Lékařů Českých.* Prague. 1958, Nov. 28, v. 97, No. 48, 1512–17. English summary.

Between 1953 and 1956 24·4% (2,000 cases) of the patients treated in the infective hepatitis wards of the author's hospital in Prague were suffering from the anicteric form of the disease. Of 2,826 persons suffering from manifest infective hepatitis 22·3% were occupied in household duties, 15·5% were factory workers and 12·3% were clerical workers; 39–64% were admitted to hospital within 1–7 days of the onset of illness, and 19–32% within 8–14 days. In 53% of the patients with anicteric hepatitis the presenting symptom was of gastro-intestinal type and in 31% it took the form of an upper respiratory infection; the course was usually mild, and 74–81% of the patients were discharged after 14 days or less. *D. J. Bauer*

FOIS, A. & VEDOVINI, F. La mononucleosi infettiva. Conoscenze attuali e contributo personale. [**Infectious Mononucleosis**] *Giorn. di Malattie Infettive e Parassit.* 1959, Mar., v. 11, No. 3, 158–65. [106 refs.]

From the University of Siena Institute of Clinical Paediatrics, the authors first give a general description of infectious mononucleosis, mentioning that liver involvement is frequent, that the specific mononuclears are indispensable for diagnosis, but that the Paul-Bunnell test may be negative more often in children than in adults. The disease is generally an acute one though chronic forms are known. Antibiotics are useless for treatment but both cortisone and prednisone are valuable.

They then give details of 18 cases seen between April and December 1956, 2 of which were of special importance. All the patients had swollen lateral cervical glands, fever to 38–39°C. was found in 17, enlargement of the spleen occurred in 14, and of the liver in 8; 3 had pseudomembranous angina, and 5 others tonsillar exudate; all had a more or less well-marked "out of sorts" feeling.

Of the 2 cases of particular importance, one had fever up to 40°C. severe melaena, the blood platelets were reduced to 110,000 per cmm., and lateral cervical glands were much swollen. A biopsy taken from one gland showed histologically an almost neoplastic appearance. The second patient had meningo-encephalitis with increase of pressure and protein in the spinal fluid and an alteration in the EEG.

Laboratory tests showed the typical mononuclears in a percentage of 6–68 in all patients, with the Paul-Bunnell test positive in 10 out of 18. Serum chromatograms showed a considerably increased $\gamma$-globulin and $\beta$-lipoprotein. The authors emphasize the extreme polymorphism of the disease and our ignorance of its cause, also the changes in the plasma constituents with the inversion of the protein formula, indicating some

condition involving the reticulo-endothelial system. The increase in $\beta$-lipoprotein merits further research.
*W. K. Dunscombe*

GIROUD, P. Épidémiologie des néo-rickettsioses. [**Epidemiology of Neo-Rickettsial Infections**] *Bull. Soc. Path. Exot.* 1958, Sept.–Oct., v. 51, No. 5, 735–41.

JADIN, J. Le traitement des néo-rickettsies. [**Treatment of Neo-Rickettsial Infections**] *Bull. Soc. Path. Exot.* 1958, Sept.–Oct., v. 51, No. 5, 742–52. [22 refs.]

DICK, G. W. A. **Epidemiology of Poliomyelitis.** *Brit. Med. J.* 1959, Mar. 7, 618–19, 2 figs.

This is a short but stimulating account of our knowledge of the factors concerned in the spread of infection and the genesis of epidemics of poliomyelitis. Children are probably the most important disseminators of virus in a community, because they excrete greater quantities and are therefore more infectious than adults. Further, there seem to be "hot" families in whom the virus multiplies well, and "cold" families in whom it multiplies poorly. If we consider a community to be made up of non-infected persons, infected poor transmitters, good transmitters, and paralysed cases, then chains of infection can most often be traced between the latter 2 groups. Quantity of virus excreted seems to be of more importance in transmission than differences in virulence between strains occurring in low and high epidemic years.

It is concluded that there is a host change which plays a large part in determining whether or not an epidemic will occur, but the nature of such a change is still unknown.
*H. Stanley Banks*

CANALIS, A., FERRO, A., BOTTACIN, L. & FRANCO, F. Episodio epidemico di poliomielite in comunità infantile chiusa. [**An Epidemic of Poliomyelitis in a Closed Community for Infants**] *Ann. d. San. Pubblica.* Rome. 1959, Jan.–Feb., v. 20, No. 1, 73–89, 3 figs. English summary.

This is a report of an outbreak of poliomyelitis which occurred in the Venetian Provincial Infants Institute in March 1956. It apparently occurred spontaneously as no case had been reported from the city, and none ascertained from the province or round about while members of the nursing staff could not give any relevant history either, even though they regularly went on leave to various parts of the province.

The outbreak affected 2 nurseries situated on the first and second floors of the nursery section; nursery I (on 1st floor) received babies up to 6 months of age, nursery II (on 2nd floor) received babies aged from 7 to 19 months. Nursery I at the time of the outbreak had 36 babies and nursery II 51: they had staff, cooking, and laundry services in common.

The first 4 cases occurred in nursery II on the same day; 6 in nursery I and 5 more in nursery II developed non-paralytic symptoms, bronchitis, diarrhoea, sometimes fever, then 1½ months later a 5th case with paralysis occurred in nursery I. 7 of the 11 with non-paralytic symptoms were excreters. Pharyngeal and rectal swabs were taken from 32 in nursery I, 55 in nursery II, and 39 staff and the results were:—nursery I, virus Type I isolated from 11; nursery II, same type virus isolated from 50; staff, Type 1 virus isolated from 3. No virus was recovered from pharyngeal swabs from babies in nursery I, nor from the staff. A second sampling 42 days later by rectal swab only on 65 babies gave the following results: Nursery I, 20 tested, 2 still positive; nursery II, 40 tested, 20 still positive; of the 5 patients with paralysis, only 1 was still positive. A 3rd sampling 3½ months after the outbreak started gave all negative results.

The serum was tested for antibodies twice on 82 babies, the first time 6 days after the outbreak, then 25 days later. In the first test 76·8% showed antibodies to Type 1, 67% to Type 2, and only 4·8% to Type 3. At the second sampling the percentages were practically the same except for a rise in Type 3 antibodies and a reduction in the number without any antibodies.

The authors emphasize the very high incidence of virus isolation, and consider that the question of excreters is very definitely affected by age, being much less in those below 6 months, while the staff also showed a very low rate. Rectal swabs were the most successful for virus isolation. They consider that the extent of the outbreak is linked to the virulence of the strain, and point out that there have been a number of outbreaks of poliomyelitis in this same Institution in the past 20 years but not in these 2 nurseries. No excreters were found 3½ months after the outbreak started.
*W. K. Dunscombe*

BRUTSAERT, P. La poliomyélite au Congo Belge. [**Poliomyelitis in the Belgian Congo**] *Soc. Path. Exot.* 1958, Sept.–Oct., v. 51, No. 5, 717–31. [20 refs.]

This is a long account of the transformation of poliomyelitis from a rarity to a serious epidemic disease in the Belgian Congo. The explanation is sought in the results of serological surveys and in the increase in the standards of living and hygiene. It is noted, too, that some epidemics have been preceded by an increase in influenza or whooping cough and the possibility that these diseases may prepare the ground for poliomyelitis is entertained.
*A. J. Beale*

GEAR, J. **The Epidemiology of Poliomyelitis in Africa.** *Ann. Soc. Belge de Méd. Trop.* 1958, Oct. 31, v. 38, No. 5, 927–37. [13 refs.]

A study of the epidemics of poliomyelitis occurring during and after the 2nd World War suggests that in the countries involved the epidemic strain of virus was more virulent than the endemic strains, that the strain had evolved in the Middle East and was spread widely in Africa and the neighbouring islands by troop movements, and that the result of introduction of the infection depended largely on the immunity status of the community. Ecological surveys of all the southern African territories and most of the neighbouring islands were carried out by using at first the Lansing mouse protection test; later, immunity to each of the 3 types of poliovirus was determined by the tissue culture protection test. It was found that most individuals, both urban and rural, had acquired antibodies to all 3 types by the 6th year of life. Europeans had a lower level of immunity than Africans of corresponding ages and many were non-immune to one or more types of the virus.

The sera of some birds and domestic animals, including cattle, yielded positive Lansing mouse protection tests. Tissue culture protection tests revealed antibodies to each of the 3 types of virus in bird sera, and the possibility of migratory birds being concerned in the ecology of human poliovirus is suggested by the seasonal incidence of the disease. Though all the South African epidemics have followed unusual rainfall favouring fly-breeding, the most recent evidence is against these insects being important epidemiologically. It is thought that the main reservoir of poliovirus is man, particularly groups of children, and that transmission is mainly by contact.

During the last 10 years an epidemic wave has involved most of southern Africa. In the 2 cities most affected African cases outnumbered European for the first time, infants being affected in the former and older age groups in the latter. The inverse correlation between the incidence of paralytic poliomyelitis and infant mortality found elsewhere probably exists also in the Union. The changing pattern of incidence probably heralds a period of severe epidemics. Virological studies on cases in southern Africa show the majority of isolations since 1956 to be Type 1. Types 2 and 3 have been isolated in the Union, the latter causing small outbreaks with high mortality. [The tables summarizing these results have been omitted.] The occurrence of several paralytic cases caused by Type 1 in a community previously relatively free indicates an impending severe epidemic.

The author believes that in countries with high living standards, though the feeding of live avirulent vaccine may involve the risk of transmission and of virulence being regained, there is less objection in a community threatened by an epidemic. This is supported by the evidence from the Belgian Congo [see this *Bulletin*, 1958, v. 33, 1022]. *T. H. Davey*

Ranzenhofer, E. R., Lipton, M. M., Dizon, F. & Steigman, A. J. **Virus Studies in Acute Aseptic Meningitis and Poliomyelitis in Louisville: 1956–1958.** *Southern Med. J.* 1959, Jan., v. 52, No. 1, 98–101.

After a brief review of the enterovirus group an account of the investigation of 124 patients with suspected viral meningitis is reported. 32 of the patients had clinically paralytic poliomyelitis. 118 stools were examined and 39 polio, 20 Coxsackie, 11 ECHO and 6 unidentified viruses were isolated. 75 cerebrospinal fluid specimens were examined, 24 from patients excreting poliovirus in the stools were negative, 3 of the remainder yielded non-polio enteroviruses. A case of paralytic disease probably due to Coxsackie A7 is mentioned [Ranzenhofer *et al.*, this *Bulletin*, 1959, v. 34, 506]. *A. J. Beale*

Sommerville, R. G. **Type-I Poliovirus isolated from a Budgerigar. Further Studies.** *Lancet.* 1959, Mar. 7, 495–6.

Sommerville *et al.* [this *Bulletin*, 1958, v. 33, 622] described the isolation of poliovirus Type 1 from a paralysed budgerigar pet of a patient with paralytic poliomyelitis. The circumstances of the isolation are reviewed and it is decided, because the isolation was made 3 times from 2 separate specimens prepared by 2 different workers, that the isolation was authentic. The virus was antigenically Type 1 poliovirus. It was inoculated into 6 budgerigars, which apart from a few days of absence of chattering in all the birds and few small areas of degeneration of motor neurones in the 4 birds inoculated intracerebrally, showed no abnormality. Similarly, no disease was found in 12 chicks. It was therefore concluded that the paralysis of the budgerigar yielding the virus was probably not due to poliovirus. A questionnaire was sent to the parents of 273 children with poliomyelitis. Replies were received from 93 paralytic and 131 non-paralytic cases, 5 and 12 respectively owned budgerigars which became ill at the time of the disease in the child. *A. J. Beale*

Dane, D. S., Dick, G. W. A. & Donaldson, S. N., with the assistance of Moya Briggs & R. Nelson. **Budgerigars and Poliomyelitis.** *Lancet.* 1959, Mar. 7, 497–8.

11 strains of poliovirus were fed and 30 days later inoculated intracerebrally into groups of 3 budgerigars. None of the birds became infected and none became paralysed although 7 out of 33 birds died from unknown causes. Only 2 birds developed poliovirus neutralizing antibodies (the titres were 1/10 and both birds were inoculated with Mahoney virus). In all, 50 birds have been examined for poliovirus neutralizing antibodies without finding any evidence of past infection. 5 " paralysed " birds were examined, 4 had suffered past bony fracture and 1 had a large renal tumour compressing the sciatic nerve. 30 out of 99 poliomyelitis patients kept budgerigars and 3 of the patients' birds died about the time of onset of the illness.

[See also this *Bulletin*, 1958, v. 33, 622.]

*A. J. Beale*

Galpine, J. F. **Some Diagnostic Problems surrounding Poliomyelitis.** *Brit. Med. J.* 1959, Mar. 7, 616–18. [15 refs.]

3 main problems in the recognition of poliomyelitis are described: (1) the distinction between non-paralytic poliomyelitis and the many other forms of " aseptic meningitis ", (2) that between the paresis of " benign myalgic encephalomyelitis " and paralytic poliomyelitis, and (3) the existence of polioencephalitis unaccompanied by paralysis. As regards the first there are now many known causes of " aseptic meningitis " including Echo viruses, Coxsackie viruses, the virus of mumps and of lymphocytic choriomeningitis, possibly the agent or agents of glandular fever, leptospires especially *L. canicola*, the tubercle bacillus and the spirochaete of syphilis, fungi, pyogenic cocci partially treated or causing a meningeal reaction secondary to an adjoining

brain abscess, and in some countries insect-borne viruses. The term non-paralytic poliomyelitis must therefore be used with caution, and in comparing rates of incidence or mortality, only paralytic cases should be counted.

Benign myalgic encephalitis has now been fairly well defined in several papers. The paresis generally shows a distinctive electromyographic pattern, but in an epidemic the distinction from poliomyelitis on clinical grounds should now be possible. Sporadic cases are apt to attract familiar labels like poliomyelitis or hysteria. In the epidemics of poliomyelitis in recent years many examples have been noted of patients with encephalitic symptoms but no paralysis [Snell *et al.*, this *Bulletin*, 1957, v. 32, 932]. It is now a reasonable supposition that the poliomyelitis virus may at times give rise to cases of this kind, as well as to cases combining encephalitis and myelitis. *H. Stanley Banks*

Riley, H. D., Jr. & Batson, R. **Poliomyelitis Problems in the Post-Vaccine Era.** *Southern Med. J.* 1959, Feb., v. 52, No. 2, 127–35, 7 figs. [30 refs.]

This is a review article concerned with problems in poliomyelitis. It is pointed out that the differential diagnosis of non-paralytic poliomyelitis embraces a host of bacterial, viral and other causes of meningitis. Even paralytic poliomyelitis presents diagnostic problems, and examples of difficulty with Guillain-Barré syndrome, myasthenia gravis and osteomyelitis are presented. There is increasing evidence that other enteroviruses may cause paralysis and a case of quadripligia and respiratory paralysis in a man of 30 associated with ECHO 5 infection without evidence of poliovirus infection is presented.

Killed poliovaccine is established as a valuable preventive measure and a course for immunization of infants is described: at age 1½ months against poliomyelitis, smallpox and pertussis; at 3 months, poliomyelitis, diphtheria, pertussis and tetanus (DPT); at 6 months, DPT; at 10 months, poliomyelitis. This has been found effective in practice [this *Bulletin*, 1959, v. 34, 609]. In view of the increasing evidence that killed poliovaccine does not prevent alimentary reinfection the use of attenuated vaccine must be considered. Similarly, more research should be undertaken with a view to replacing monkey kidney cells by continuous cultivated cell lines for the production of poliovaccine. *A. J. Beale*

Celers, J., Drouhet, V., Schwartz, D. & Soulé, S. L., with the collaboration of G. Said & L. Trocellier. Études immunologiques sur la poliomyélite. III.—Recherche de facteurs liés à l'acquisition des anticorps antipoliomyélitiques. **[Immunological Studies on Poliomyelitis. III. Study of Factors Connected with the Acquisition of Antibodies]** *Rev. d'Immunologie.* 1958, Oct.–Dec., v. 22, Nos. 5/6, 530–45, 2 figs.

Between November 1956 and February 1957 sera were obtained from 197 children living in and around Tours who were born between 1/10/51 and 31/3/52. Roughly equal numbers of children had antibodies to one or other of the 3 types of poliovirus and were without antibodies. The influence of various factors on the acquisition of antibodies was investigated. It was found that there were marked variations in the proportion of children with antibodies in the communities around Tours. Also, antibodies were more prevalent in the lower social classes (measured by fathers' occupation and educational background, living area, presence of a garden, and number of persons per room) in children from families with many contacts with other people and in those from homes with more primitive sanitation. However, these factors were not considered adequate to explain all the differences. Other factors, for example the virulence of the particular strains and the climatic conditions during the period of virus spread, are considered important but rather difficult to investigate.

[For earlier parts of this study, see this *Bulletin*, 1958, v. 33, 103 *bis*.] *A. J. Beale*

Salk, J. E. **Poliomyelitis Vaccine Preparation and Administration. Analysis of Basic Premises and Current Practices.** *J. Amer. Med. Ass.* 1959, Apr. 18, v. 169, No. 16, 1829–38. [15 refs.]

Poliovaccine has now been in use for about 5 years on an increasing scale, and it has become apparent that some individuals who have had 3 doses of vaccine have nonetheless contracted paralytic poliomyelitis. In this paper Dr. Salk discusses and describes investigations into the reasons why these failures of poliovaccination occur. 5 theoretical explanations are considered: 1. That the potency of the vaccines at present in use is inadequate. 2. That the individuals who contract poliomyelitis may be particularly unresponsive to vaccine. 3. The antibody titres induced by the vaccine may wane with time. 4. The virus may have reached the central nervous system by a route other than the bloodstream thus by-passing the antibodies present in the serum. 5. The particular paralysing agent may not have been poliovirus. The evidence suggests that the major cause of the vaccine failures is due to poliovaccines of less than optimal potency. Antibody levels appear to be well maintained for one or two years after 3 doses of poliovaccine, either of Salk's reference vaccine A or commercially available batches of vaccine [this *Bulletin*, 1958, v. 33, 824]. However, the effectiveness of reference vaccine A given in a dose of 2, 1 or ½ ml. is greater than a dose of ¼, ⅛ or 1/16 of an ml. In a study carried out in May 1956 among 4,417 children in the first 3 grades of school, it was found that 99% had antibodies to all 3 types of poliovirus after 3 doses of vaccine but in a similar study carried out in the spring of 1958, it was found that 9% had no detectable antibodies to Type 1, 0·5% lacked them to Type 2 and 18·7% to Type 3 after 3 doses of vaccine. [These data are preliminary. It is said that a more careful check has revealed that some of the children had had more than 3 doses and that others had had less or maybe even no vaccine at all. The more detailed analysis of these figures is promised later.] However, the children that failed to respond to 3 doses of vaccine were recalled and given a fourth dose. It was found that these children nearly all responded to a fourth dose either of a special lot of high potency vaccine or to lots of vaccine that were commercially available in Pittsburgh in 1958. It has also been found that the potency of the antigen given in the primary course conditions to some extent the response to a subsequent booster dose. If the vaccine used for the primary dose is of poor quality then the booster response will be much poorer than after potent primary immunization. Preliminary studies are also reported on 103 patients who were considered to have paralytic poliomyelitis and who had had 3 doses of poliovaccine. It is stated that the complete clinical records are not yet available but that these suggest that not all the cases were really paralytic poliomyelitis. However, from the 103 patients, 75 agents were identified, 39 Type 1 polioviruses and 15 Type 3 polioviruses and 20 other enteroviruses as follows: Coxsackie A9, 3; B3, 1; B4, 2; B5, 7 and ECHO 9, 7. There was in addition 1 patient who yielded Type 1 and Type 3 virus. It is concluded that as an interim measure it is probably advisable to give a fourth dose of poliovaccine but it is pointed out that the ultimate solution to the problem must depend upon the availability of vaccines of greater potency. It is pointed out that this must be possible since the vaccines that were prepared in 1955 both in Dr. Salk's laboratory and by some manufacturers were capable of giving a satisfactory immunological response in children.

*A. J. Beale*

MOLNER, J. G., BRODY, J. A. & AGATE, G. H. **Detroit Poliomyelitis Epidemic—1958. Preliminary Report.** *J. Amer. Med. Ass.* 1959, Apr. 18, v. 169, No. 16, 1838–42, 4 figs.

There was a major epidemic of poliomyelitis in Detroit in 1958. A total of 312 paralytic and 315 non-paralytic cases was reported. This paper is a preliminary account of the epidemic. Virological studies showed that most of the paralytic cases were due to Type 1 or Type 3 poliovirus but only 25% of the non-paralytic cases were due to poliovirus infection. In previous years epidemics of poliomyelitis in Detroit have shown little selectivity by region or race, the disease was widespread throughout the area generally affecting the wealthier suburbs at least as severely as the centre of the town. This epidemic, however, occurred predominantly in the overcrowded down-town area and the paralytic attack rate of the non-white population was 18 times that of the whites. The concentration of cases in the down-town area was less pronounced for the non-paralytic cases. 61·5% of the patients with paralytic poliomyelitis were under 5 years of age and most of them were under the age of 3 years whereas the non-paralytic cases reached a plateau of incidence between the ages of 2 and 9 years. There were 229 cases of paralytic poliomyelitis in people who had had no poliovaccine but only 15 among those who had had 3 or more doses. Also, none of the 22 patients who died had had 3 doses of vaccine. Of 334 unvaccinated patients reported as having poliomyelitis 70% were paralysed, while of 136 cases of poliomyelitis among those who had had 3 or more doses 11% were paralysed. Before the epidemic, efforts to protect the public against poliomyelitis had been made in Detroit but the results of the epidemic revealed that they had not been very successful particularly in the central area of the city in the lower socio-economic groups and principally in the young pre-school children. As a result of the epidemic poliovaccine was administered on a very large scale. Over 600,000 doses of vaccine were given by official agencies and it is estimated that approximately 3 times as many were administered by private physicians over a period of 2 months. The authors warn other public health workers to look to their poliovaccination programmes lest a similar fate as that of Detroit befalls their communities.

[Although the vaccine in use in Detroit was presumably of suboptimal potency, judging by the results of Salk in Pittsburg in 1958 (see above), there seems little doubt that it did have a protective effect.]

*A. J. Beale*

ŽÁCEK, K., VONKA, V., ADAM, E. & ADAMOVÁ, V. **The Antibody Response in Children vaccinated with the Poliomyelitis Vaccine injected in Different Ways.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 1, 60–66, 2 figs.

During 1957 mass poliovaccination was carried out in Czechoslovakia by the intradermal route. An attempt was made to determine whether the intradermal route was as satisfactory as the subcutaneous (with a batch of Canadian vaccine). The children tested were all in orphanages where the rate of natural acquisition of antibodies was high. All were either triple negative or only had Type 3 antibodies. Excluding the children from one nursery the response to vaccination was similar by either route. After the third intradermal dose (8 months after the primary course) 7 out of 17 previously triple negative children lacked antibodies to Type 1 and similarly 1 out of 13 children inoculated subcutaneously failed to respond to 3 doses. All the children in the excluded nursery were inoculated intradermally and none out of 6 responded to Type 1. The children in this nursery were 1–2 years younger, had a higher standard of hygiene and lower rate of acquisition of poliovirus or Coxsackie A9 and ECHO 9 antibodies than the other children. The authors point out that these factors have a marked influence on the assessment of the antigenicity of poliovaccine.

*A. J. Beale*

PERKINS, F. T., YETTS, Risha & GAISFORD, W. **Response of Infants to a Third Dose of Poliomyelitis Vaccine given 10 to 12 Months after Primary Immunization.** *Brit. Med. J.* 1959, Mar. 14, 680–82, 3 figs.

Previously the authors have described the response of children to 2 doses of poliovaccine, the first dose being given at 1, 6 and 10 weeks of age [this *Bulletin*, 1958, v. 33, 1021]. The results were considered disappointing, mainly because of the effect of maternally transmitted antibody. This antibody may have prevented a primary response or merely masked it. The test of these alternatives was applied by giving a booster dose 10–12 months later to 80 of the children. 17 of these had very high levels to one or other type probably from natural infection and were excluded from the assessment. The booster response of the oldest children was better than for the younger, and the response for Types 2 and 3 better than Type 1. Children who had responded to the primary course in general gave a better response than children who had not responded, although a proportion of those with maternal antibodies to a titre of 1/32 to 1/1,024 were evidently sensitized, *i.e.* the primary response was masked not prevented. The booster responses for Types 2 and 3 for children inoculated at 10 weeks were tolerable, only 2 (out of 18 in group) having titres of 1/64 or below for Type 2 and 1 for Type 3. For Type 1, on the other hand, although only 2 failed to respond completely in the 10-week group compared with 5 out of 23 in the 6-week and 17 for the group vaccinated at 1 week, an additional 5 had titres of 1/64 or less. It was concluded that the response to polio-vaccination at 1, 6 or 10 weeks is too poor, both immediately and for sensitization to a booster dose, to be recommended for general use. *A. J. Beale*

PERKINS, F. T., YETTS, Risha & GAISFORD, W. **A Comparison of the Responses of 100 Infants to Primary Poliomyelitis Immunization with Two and with Three Doses of Vaccine.** *Brit. Med. J.* 1959, Apr. 25, 1083–6, 3 figs.

The authors have previously shown that infants under 10 weeks old respond poorly to 2 doses of 1 ml. of killed poliovaccine. This is due to the inhibiting effect of maternal antibody and to the immunological immaturity of the young children. In this study an attempt to secure better results has been made by employing either 2 or 3 2 ml. doses at 4-week intervals in 1-week-old children and 3 1 ml. doses on a similar schedule for 16-week-old children. The level of maternally transmitted antibodies and their half-life (21 days) was similar to that reported previously [this *Bulletin*, 1958, v. 33, 1021]. The response of 1-week-old children remained poor even with the increased dosage especially for Type 1. The numbers without maternal antibody responding were: 4 out of 8 Type 1, mean titre 1/6; 10 out of 10 Type 2, mean titre 1/274; and 9 out of 10 Type 3, mean titre 1/157. In 16-week-old infants 3 1 ml. doses gave better results than 2 doses. This is illustrated by the Type 1 results: after 2 doses, 7 of 22 responded with a mean titre of 3 and after 3 doses, 20 of 24 responded with a mean titre of 23. However, for children with maternal antibodies after 3 doses, 9 of 25 responded to Type 1, 18 of 29 to Type 2 and 20 of 22 to Type 3. Judging from previous results [see above] part of the apparent poor effect in those with maternal antibodies is a masking of the response subsequently revealed by the good response to a booster dose and partly a real inhibition. The authors conclude as a result of their studies that in order to achieve satisfactory immunization it is best to wait till maternal antibodies have disappeared. They therefore advise starting polio-vaccination between 6 and 9 months and employing 3 doses each of 1 ml. at monthly intervals for the primary course. The value of the third dose is probably partly explicable as the effect of a greater dose of antigen and partly due to a drop in maternal antibodies which occurs after another 4 weeks delay before the third dose is given.

*A. J. Beale*

MEDICAL RESEARCH COUNCIL. Biological Standards Control Laboratory. **Antibody Response of Adolescents and Adults to a Booster Dose of Poliomyelitis Vaccine.** *Brit. Med. J.* 1959, Mar. 7, 609–13, 7 figs. [10 refs.]

This report continues the valuable series of investigations conducted under the auspices of the Medical Research Council into the performance of British poliomyelitis vaccine in the field. Previously [this *Bulletin*, 1958, v. 33, 288] it has been shown that the response of children under 10 years of age to a booster dose of poliovaccine was very satisfactory, although a few failed to show a booster response to the Type 1 component. These few children had no detectable antibodies at the time of the third inoculation. In the present investigation 86 schoolboys and 25 adult medical personnel were used for further trials of the antibody response to British vaccine. The 2 primary doses were given with an interval of one month between them and the booster dose was given either 6, 9 or 12 months later. The time of giving the booster dose did not appear to have any significant effect upon the response.

For Types 2 and 3 the response of the adults to the booster dose was very satisfactory and comparable to the results reported earlier although 4 people had no antibodies to the Type 2 component at the time of the third dose. However, response to Type 1 was much less satisfactory. About one-third of the individuals lacked antibodies to the Type 1 component at the time of the third inoculation and these people responded in general in very much the same way as individuals who had had no primary course but did have antibodies to the Type 2 component. Efforts were made to increase the response to the Type 1 component by increasing the number of doses and by using 2 experimental vaccines which had approximately twice and three times the potency of the basic trivalent vaccine. The use of a fourth dose appeared to give a booster effect.

The fortified Type 1 vaccines produced greater potency, thus the normal batches of vaccine gave a geometric mean titre to Type 1 of 1:20 to 1:32, whereas the vaccine containing respectively 2 and 3 times the usual amount of Type 1 gave geometric mean titres of 1:60 and 1:151. It it not yet known whether the booster response after these fortified vaccines will be satisfactory, although this result can clearly be expected. The authors, therefore, note that it would be desirable to see at least a 3-fold increase in the potency of the Type 1 component of the vaccines currently being prepared. A better response could also be achieved by giving a fourth dose but this is administratively difficult. Alternatively, it could be achieved by the use of a greater individual dose and the authors suggest 2 1·5 ml. doses for adolescents with a 1 ml.

booster dose in all age-groups. They suggest that their results indicate that the immunity following the primary course of vaccine may be quite short-lived and in this connexion it is salutary to remember that the trials showing the efficacy of poliovaccine in preventing paralysis were conducted within 7 months of giving 2 doses of vaccine and it was found that the antibody response to a booster dose began in 5 to 6 days in those with prior antibodies (whether from natural infection or vaccination) whereas if there were no prior antibodies the response was delayed till 7 or more days. Finally, the authors suggest that if potent killed vaccines do not become available then attenuated vaccines will have to be considered, either alone or in conjunction with the killed vaccine. *A. J. Beale*

KNOWELDEN, J. **Present Situation with Formalin-Killed Poliomyelitis Vaccine.** *Brit. Med. J.* 1959, Mar. 7, 620–21. [10 refs.]

In this paper Dr. Knowelden makes a plea for the continued use of the clinical trial in filling the gaps in our knowledge of poliomyelitis vaccination. He points out that only 2 controlled trials have been carried out, one in North America by FRANCIS *et al.* [this *Bulletin*, 1955, v. 30, 663] and the other by the Medical Research Council in England [*ibid.*, 1957, v. 32, 832]. In the American trial the vaccine was found to be 72% effective against the paralytic form of the disease. Similar results were obtained in the smaller English trial but because of its small size it was not possible to estimate the degree of protection accurately. For non-paralytic poliomyelitis even in those cases confirmed by virus isolation the protection did not reach the levels of statistical significance. Moreover, it has transpired recently that killed vaccine, or at least 2 doses of it, does not prevent subclinical alimentary infection with poliovirus. It is concluded, therefore, that however extensive the programme with killed virus vaccine becomes it is unlikely to reduce the reservoir of poliovirus in the community. [It is still too early to assert this dogmatically because the antibody titres of most of the people who have shown alimentary infection after killed vaccine have been rather low either because they have only had 2 doses or because of the low potency of the vaccine used.]

The evidence for a third dose of vaccine is reviewed and considered overwhelming. It is, however, all of a serological nature and suffers from the defect that the antibody level conferring protection is unknown. It is as yet unknown how long protection against paralytic disease lasts after the primary vaccination with 2 doses (in both the British and American trials a period of 7 months after vaccination was used) and no controlled trial of the 3-dose schedule has been made. It is therefore not known definitely that it confers superior protection [this can surely be inferred from the serological results]. Dr. Knowelden clearly believes that answers to these questions could be obtained by appropriate clinical trials, and would prefer to see an attempt made to answer some of them before important decisions are taken about poliovaccination programmes in ignorance. *A. J. Beale*

DICK, G. W. A. & DANE, D. S. **Live Poliomyelitis Vaccine.** [Correspondence.] *Brit. Med. J.* 1959, Mar. 28, 853–4.

In this letter Drs. Dick and Dane comment on 4 aspects of SABIN's recent paper in the *Brit. Med. J.* [this *Bulletin*, 1959, v. 34, 835].

1. Neurotropism of excreted virus. They re-examined the most neurotropic virus excreted in the trial of CLARKE *et al.* [*ibid.*, 1959, v. 34, 201] from volunteer 1203. This strain was subcultured once in high bicarbonate medium and found to be still in the avirulent range, *i.e.* less virulent than strains isolated from paralysed patients but similar to avirulent strains isolated in nature. Dr. Sabin suggests that epidemics may be terminated by the occurrence of avirulent mutants; the authors point out that a reversion to virulence may occur at the start of an epidemic. The crux of the matter is whether vaccine strains can revert to full virulence and the authors would like to see this possibility more fully examined before large scale trials of attenuated vaccine are carried out.

2. Persistence of immunity and its relation to resistance of the alimentary tract. The durability of alimentary immunity is questioned because both Sabin and Clarke *et al.* were able to infect some naturally immune people. The present authors prefer to measure immunity by circulating antibodies, but as yet there is no evidence of the duration of antibodies after the use of Sabin's present strains.

3. It is believed that adequate immunization with potent killed vaccine may well cause the elimination of poliovirus from the community. Already Sabin found that inadequate vaccination prevented multiplication of poliovirus in the pharynx. Although Sabin dismissed pharyngeal virus as unimportant epidemiologically, it is pointed out that it may well be very important since exchange of saliva is more frequent than of faeces among children.

4. The authors believe that field trials in " suitable " countries would almost certainly do less harm than good. In view of unknown risks they advocate " non-specific caution " and are reinforced in this view by Sabin's finding that COURTOIS *et al.* [*ibid.*, 1958, v. 33, 1022] fed poliovirus contaminated with an unknown virus to 200,000 people in the Congo. *A. J. Beale*

BUSER, F. & SCHÄR, M. Schutzimpfung gegen Poliomyelitis mit lebenden avirulenten Viren. Vorläufige Mitteilung. [**Poliomyelitis Vaccination with Live Avirulent Virus**] *Schweiz. med. Woch.* 1958, Dec. 20, v. 88, No. 51, 1282–4, 3 figs. [31 refs.]

An investigation has been made of the immunizing effect of oral administration of the Chat strain of Type 1 poliomyelitis virus in 115 persons (children and their parents). No symptoms of illness were observed in the 2 months following vaccination. The virus was recovered from the stools of 86 persons 10 days after administration. 58 of 60 persons who were initially seronegative developed Type 1 neutralizing antibody in titres of 50 or higher. *D. J. Bauer*

FOWDEN, A. **Sensitivity to Penicillin in British Poliomyelitis Vaccine.** [Memoranda.] *Brit. Med. J.* 1958, Oct. 4, 835.

British poliomyelitis vaccine contains a small amount of penicillin and to a question on the safety of giving it to a penicillin-sensitive person the reply in a previous issue of this journal was "To our knowledge no report has been made of any case of sensitization to the antibiotics" (*Brit. Med. J.*, 1958, v. 1, 1555). In view of this reply a case report is given here of the symptoms and signs which followed the injection of 1·0 ml. of the British vaccine in a boy aged 12 years who was known to be sensitive to penicillin. A few hours after the injection a sparse, itchy rash appeared on the trunk and limbs with the rapid development of vesicles. When seen next day he had severe frontal headache and felt lethargic and generally unwell. There were no abnormal signs on examination. Treatment with antihistamine was begun with good results but 3 days after the injection he complained of a tightness of the chest and breathlessness and bronchospasm was present but was quickly abolished by antispasmodic treatment. The respiratory and skin conditions settled down but headache and malaise persisted for about 10 days. The skin condition "must be considered as part of a sensitivity reaction" and the "bronchospasm may have related". The origin of the severe and persistent headache "must be conjectural". It is noted that signs and symptoms of mumps appeared 24 days after the injection. *M. E. Delafield*

LIU, O. C., CARTER, J. E., SANDERS, B. E., SMITH, E. C. & HAMPIL, Bettylee. **A Study on Serotherapy of Poliomyelitis in Rhesus Monkeys.** *Brit. J. Exper. Path.* 1959, Apr., v. 40, No. 2, 133–44, 4 figs. [20 refs.]

The authors have previously reported that a powerful immune serum to Type 1 poliovirus made in rabbits confers a significant degree of protection to monkeys inoculated with a small dose of Type 1 poliovirus (Mahoney strain) intraspinally when given before the onset of symptoms [this *Bulletin*, 1958, v. 33, 892]. The work has now been extended to cover the use of serum after the appearance of symptoms. 3 sorts of experiment were done. In the first, between 10–16 TCD50 of Mahoney virus were inoculated intraspinally and 48 hours later when symptoms (paralysis and pyrexia) were present the monkeys were given 20 ml. of antiserum (titre 1/75,000) intravenously. 7 out of 9 control animals died, while only 1 out of 15 treated animals died. Moreover, the treated animals showed much less paralysis, which was always confined to the lower limbs and often to one limb. In the second group of experiments 5 × $10^5$ TCD50 of Mahoney virus was inoculated intracerebrally and between 3 and 7 days later animals were given 5, 10 or 15 ml. per kgm. of poliomyelitis antiserum. The infection was not usually lethal in control animals who had fever for a day or two followed by an afebrile period of 1–4 days followed by a second peak of fever. They developed unsteadiness and tremor and became sluggish and later developed paralysis of face, neck and upper limbs. Animals treated with 15 ml. per kgm. did not become paralysed whereas the smaller doses were ineffective. In these experiments the monkeys which received 15 ml. of serum had an antibody titre of 1:17,700 10 minutes after treatment which closely approximates to the theoretical expectation from the dose given.

Finally, with a view to the application to the therapy of human poliomyelitis, human gamma globulin containing high levels of neutralizing antibodies to all 3 Types of poliovirus was prepared. 39 volunteers were immunized with poliovaccine and then gamma globulin was prepared from the plasma. The titre of the plasma post vaccination was Type 1 1:9,700; Type 2 1:13,400; Type 3 1:6,000, and of 16% gamma globulin solution prepared from it Type 1 1:75,050, Type 2 1:86,280 and Type 3 1:52,130. There were considerable losses of antibody during the preparation of gamma globulin, the yield being 30–40%. 3 dose levels were employed in monkeys 0·3, 0·6 and 1·5 gm. per kgm. given intravenously immediately after 100 TCD50 of Mahoney virus intraspinally. No effect was noted with 0·3 or 0·6 gm. but with 1·5 gm. none of 3 animals died and only 1 had partial lower limb paralysis, whereas all the control animals in this experiment were completely paralysed and died. About 25% of the animals developed shock-like symptoms after the intravenous inoculation of gamma globulin. Apart from this it is considered that serotherapy may prove of value for the treatment of poliomyelitis in man. *A. J. Beale*

GORDON, R. B., LENNETTE, E. H. & SANDROCK, Rachel S. **The Varied Clinical Manifestations of Coxsackie Virus Infections. Observations and Comments on an Outbreak in California.** *Arch. Intern. Med.* 1959, Jan., v. 103, No. 1, 63–75, 7 figs. [36 refs.]

An outbreak of Coxsackie B-5 virus infection in Shasta County, Northern California, which occurred in 1956 was investigated. 3 distinct varieties of clinical manifestation were seen, all apparently due to Coxsackie B-5 infection. The most common manifestation was pleurodynia, the frequency of nausea and vomiting in addition to chest or abdominal pain is stressed. Meningitis occurred either alone or in combination with pleurodynia. Although after the report of JAVETT *et al.* (*J. Pediatrics*, 1956, v. 48, 1) the authors were on the look-out for myocarditis no cases were seen. However, 7 cases of pericarditis are reported probably due to Coxsackie B-5 infection. 1 had Coxsackie B-5 in the stools and all had high titres of CF antibodies to Coxsackie B-5 virus in convalescence. The patients with pericarditis also had pleurodynia and 3 also had a pleural effusion.

[This is a most interesting paper. Evidence for the association of Coxsackie B infection and acute benign pericarditis has been reported by several authors: FLETCHER & BRENNAN, this *Bulletin*, 1957, v. 32, 834; KAGAN & BERNKOPF, *Ann. Paediat.*, 1957, v. 189, 44;

WEINSTEIN, this *Bulletin*, 1957, v. 32, 1136; MCLEAN *et al.*, *Canadian Med. Ass. J.*, 1958, v. 79, 789.]
*A. J. Beale*

ST. GEME, J. W., Jr., PRINCE, J. T., SCHERER, W. F. & KRIVIT, W. **A Clinical Study of an Exanthem due to Echo Virus Type 9.** *J. Pediatrics.* St. Louis. 1959, Apr., v. 54, No. 4, 459–67. [22 refs.]

The association of ECHO virus type 9 with an exanthematous illness was established in 13 patients: 1 was an infant, 6 were aged 1–5, 3 aged 6–10, and 3 were adults. The rash resembled that of rubella but its main incidence was on the face. Fever was present in all patients either before or with the rash. Upper respiratory symptoms were present in 6 patients but were not marked. Cervical lymphadenopathy was present in 7: headache was present only in the 3 adults. There was a strong family incidence and the incubation period appeared to be about 1 week. The mother of 4 patients with a rash developed a febrile illness with meningismus but no rash: she had a 64-fold rise in neutralizing antibody against ECHO 9 virus. [The association of ECHO virus with abacterial meningitis with or without rash is well known: this article stresses rather the frequency of a rubella-like illness with rash but no meningismus.] *A. B. Christie*

AITKEN, T. H. G. & ANDERSON, C. R. **Virus Transmission Studies with Trinidadian Mosquitoes. Part II. Further Observations.** *Amer. J. Trop. Med. & Hyg.* 1959, Jan., v. 8, No. 1, 41–5. [12 refs.]

10 species of mosquito were used: *Culex fatigans* and *Aëdes aegypti* were laboratory-bred; *Trichoprosopon digitatum* were bred from wild-caught larvae; the other species were wild-caught adults. They were infected by inoculation into the thorax with infected mouse brain suspensions. After varying extrinsic incubation periods they were allowed to feed on 2-day-old chicks or 2-day-old mice.

Ilheus virus was transmitted by all 6 species tried (*Aëdes aegypti, Aëdes scapularis, Aëdes serratus, C. fatigans, Psorophora albipes* and *P. ferox*) after incubation periods of 6–14 days, each of them by a single mosquito. Several chicks which circulated virus failed to develop detectable neutralizing antibody a month later.

St. Louis virus was also transmitted by all species tried (*Aëdes aegypti, Aëdes serratus, C. fatigans, Mansonia arribalzagai, M. venezuelensis* and *P. ferox*) after a 7–11-day incubation period. Single mosquitoes transmitted with all except *A. serratus.* All chicks which circulated virus developed antibody.

Only one transmission of Mayaro virus was achieved —with *Aëdes scapularis* after a 7-day incubation period. 6 other species harboured virus for at least 12 days but only 3 species survived long enough for biting experiments. 2 groups of *C. fatigans* at 7 days and a single one at 12 days failed to transmit.

[For Part I, see this *Bulletin*, 1958, v. 33, 1194.]
*C. E. Gordon Smith*

IZOTOV, V. K. & BAROIAN, O. V. **Detection of the Virus of Tick-Borne Encephalitis by Fluorescence and Electrophoresis. (Preliminary Communication.)** *Problems of Virology.* London. 1958, v. 3, No. 4, 236–9, 3 figs. [Translated from Russian.]

Brain suspensions of mice infected with the Sofin strain of Russian spring-summer virus and of normal mice were subjected to paper electrophoresis and then stained with acridine orange. 2 fluorescent areas could be demonstrated, (1) at the site where the material was placed on the paper and this was much more intense with the infected brain; (2) 2–3 cm. towards the anode. Treatment of the brain suspension with immune serum before electrophoresis neutralized the phenomenon. [The observations are interesting but the claim that the presence of encephalitis virus can be established in this way in 18 hours seems hardly justified at this stage.]
*C. E. Gordon Smith*

FEDOROV, J. V., IGOLKIN, N. I. & TIUSHNIAKOVA, M. K. **Some Data on Virus-Carrying Fleas in Areas of Tick-Borne Encephalitis and Lymphocytic Choriomeningitis.** *Med. Parasit. & Parasitic Dis.* Moscow. 1959, v. 28, No. 2, 149–52. [In Russian.]

The English summary appended to the paper is as follows:—

"Investigations were carried out in the forests of the Tomsk and Guriev districts in Western Siberia. The flea fauna in the localities is represented by 23 species (12 genera). 1367 fleas were subjected to a virological examination.

"From the fleas Paiaeopsylla sorecis one virus strain of tick-borne encephalitis was isolated, while the fleas collected on red voles (Clethrionomys glareolus) were found to be infected with the virus of lymphocytic choriomeningitis."

MASI, A. T., TIMOTHEE, R. A. & ARMIJO, R. Estudio epidemiológico de un brote hídrico de fiebre tifoidea. **[Epidemiological Study of a Water-Borne Outbreak of Typhoid Fever]** *Bol. Oficina Sanitaria Panamericana.* 1958, Oct., v. 45, No. 4, 287–93, 3 figs. English summary.

This paper describes an outbreak of 23 cases of typhoid fever in the modern town of Ponce, Puerto Rico. The population is 99,422. The cases occurred within a period of 24 days (August 24 to September 17). All patients, except 3, were under 15 years of age and all cases were mild. The organism was phage typed and found to be degenerated Vi, which is normally rare in the city. The cases were concentrated in 2 central areas, 6 being in one street, and the incidence was 14 times greater in these 2 areas than in the rest of the city. Apart from water the only article of food or drink taken by the majority of the patients was pasteurized milk of unquestioned quality. Bacteriological examination of food handlers was negative.

The public water supply is from 5 deep wells and a reservoir and is chlorinated by an automatic mechanism. The water pressure in the centre of the city is low and as, during the dry season, consumers can only draw water at fixed times the water in the distribution pipes is sometimes stagnant for some hours. There are many inter-connexions within the distribution system.

On August 12 the island was struck by a severe hurricane and many refugees crowded into the city, mainly the central area, from the surrounding country. The rare phage, degenerated Vi, had previously been isolated in one of the areas from which they came. The electricity supply failed and the normal routine of testing the public water supply was disturbed. The first samples taken after the resumption of testing showed no contamination but on the next day, August 16, the coliform content was 16 per 100 cc. A similar result was obtained on August 20 and again at another sampling point on August 22. Maps show that the distribution of the cases coincided with the area served by the contaminated water. Coliform contamination had been found previously in this section of the water distribution service but it had not been regarded as dangerous. House-to-house inspection in the district showed many sanitary defects and opportunities for contaminating the water supply. For example there was a private well connected directly and without valves with the public service and water pipes adjoining drains were found.

The English summary of this paper is particularly good. *Allen Daley*

Sobol, H. **Rheumatic Endocarditis complicated by Typhoid.** *J. Amer. Med. Ass.* 1959, Apr. 25, v. 169, No. 17, 1998–2000. [10 refs.]

" In a rare case, rheumatic heart disease was present with typhoid. Early diagnosis of bacteremia in patients with chronic rheumatic valvular disease is important."

Steinmetz, P. R. **Typhoid Fever obscured by Inadequate Chlortetracycline Therapy. Report of a Case.** *New England J. of Med.* 1959, Apr. 9, v. 260, No. 15, 765–6.

A naval technician aged 19 on a United States vessel in the Mediterranean developed a febrile illness on May 17, 1958, and came under medical care on May 20. Leucopenia and splenomegaly were fairly early signs but otherwise there were no diagnostic symptoms other than continued pyrexia. Repeated blood, stool and urine cultures were negative. Agglutination to the typhoid group was negative on June 10 but was positive to *Salm. typhi* O at 1/40 on June 18: on June 30 agglutination to typhoid O and H antigens was positive at 1/640. Blood culture was positive for *Salm. typhi* on June 27 and treatment with chloramphenicol was begun with effect on June 28. Scrutiny of the records at this stage revealed that the patient had had a 5-day course of chloramphenicol, 1 gramme per day, from May 22 and the author felt that this course had brought about temporary improvement and had been responsible for the negative cultures and possibly the late development of antibodies. He regards as remarkable the absence of respiratory and gastro-intestinal symptoms in a case of typhoid fever. Others might have regarded the positive O agglutination on June 18 along with leucopenia and splenomegaly as strongly suggestive of typhoid fever. *A. B. Christie*

Shearer, Lois A., Browne, A. S., Gordon, R. B. & Hollister, A. C., Jr. **Discovery of Typhoid Carrier by Sewage Sampling.** *J. Amer. Med. Ass.* 1959, Mar. 7, v. 169, No. 10, 1051–5, 1 map. [11 refs.]

Moore's sewage swabs and the method described by him for the detection of typhoid carriers [this *Bulletin*, 1949, v. 24, 187; *ibid.*, 1950, v. 25, 837; *J. Hygiene* 1952, v. 50, 137] were successfully employed in the investigation of sporadic cases of typhoid fever that occurred in a community of about 2,000 people living in the High Sierra country of California over the previous few years. As there was no epidemiological evidence to indicate any particular area where the carrier might be found, the complete sewage system of the whole township was " swabbed ". Within 3 days of setting the swabs *Salmonella typhi* began to be isolated from swabs in certain of the manholes and the contaminated sewage was eventually traced to a particular " block ". The phage-typing of the *Salm. typhi*, undertaken in conjunction with the Communicable Diseases Center, Georgia, showed that the type isolated was unusual as a U.S.A. type, but that its origin could be related to a source in Holland. Detailed enquiries of all the residents in the " block " revealed that a German immigrant who had, 50 years previously, stayed in a house in Germany, where there had been a case of typhoid fever in a person from Holland, was now living in this " block ". This man, when examined bacteriologically, was found to be excreting *Salm. typhi* of the same phage-type as that associated with the various outbreaks in the community concerned and was justly considered to be the source of the infection.

*H. J. Bensted*

Polanetzki, U. & May, G. Zur Dauer der Bakterienausscheidung bei Enteritiskeimträgern. **[The Duration of Excretion of Enteritis Bacteria by Carriers]** *Desinfektion u. Gesundheitswesen.* 1959, Mar., v. 51, No. 3, 33–8. [26 refs.]

This paper contains a general discussion of the hygienic problems associated with the carrier state and the duration of bacterial excretion by patients and by healthy individuals. It is based on the experience of 357 persons from whom enteritis organisms of different groups were isolated during 1954–8 in the Hygiene Institute of Frankfurt a. Main. A table sets out the duration of bacterial excretion in these persons. There are case histories of the 11 persons who continued to excrete 6 months after the first isolation of a particular enteritis organism. Emphasis is also placed on the importance of the so-called " late excreters " who continue to excrete 10 weeks after clinical convalescence. A list is given of the particular salmonellae isolated from these patients. *M. E. Delafield*

Humbert, R. Diagnostik und Therapie der Salmonellen-Dauerausscheider. Bericht über 100 Patienten. **[Diagnosis and Treatment of Chronic** *Salmonella* **Excreters (Report of 100 Cases)]** *Deut. med. Woch.* 1959, Apr. 10, v. 84, No. 15, 742–4, 749–52, 775. [61 refs.]

The English summary appended to the paper is as follows:—

"It is pointed out that almost all salmonella carriers harbour the organism in the biliary tract. This chronic bacterial infestation usually causes cholecystitis and cholelithiasis. Conservative treatment with antibiotics generally fails to cure the carrier state, although penicillin in bactericidal doses is sometimes effective. The treatment of choice combines cholecystectomy with administration of antibiotics. Cholecystectomy without antibiotics was successful in only 7 of 20 cases, while the combination was successful in 14 of 24. Tetracycline or oxytetracycline seemed to be best. It is thought possible that the addition of high doses of penicillin will further improve results. Choledochotomy and drainage is advised only in the presence of cholangitis and common duct stones. Some of the socio-economic problems of the chronic carrier stage are discussed."

BARR, M., SAYERS, M. H. P. & STAMM, W. P. **Intradermal T.A.B.T. Vaccine for Immunisation against Enteric.** *Lancet.* 1959, Apr. 18, 816–17.

Before the 2nd World War intradermal TAB vaccine was being recommended, at least for re-inoculations, for the United States Army troops (SILER, J. F. & DUNHAM, G. C., *Amer. J. Pub. Health*, 1939, v. 29, 95). The intradermal dose of vaccine contained a total of 100 million organisms, which was considered adequate to boost the existing immunity from the primary subcutaneously administered TAB vaccine, and at the same time to reduce significantly the troublesome local and general reactions caused by the larger doses given subcutaneously.

Some doubt existed about the value of the intradermal method for primary inoculations although it was agreed that the reactions after its use were generally less severe. Since the war, however, reports from several sources have been more favourable and recently a Working Party set up by the British Army Pathology Advisory Committee has been re-examining the problem with a view to extending the use of the intradermal method to the combined prophylactic against the enteric group of fevers and tetanus (TABT) and this paper records the results of the antibody responses to both the enteric and tetanus components of the vaccine.

The original formal tetanus toxoid was not potent enough to use in doses of 0·1 ml., but with a casein hydrolysate medium [MUELLER, J. H. & MILLER, P. A., this *Bulletin*, 1954, v. 29, 880] suitably high Lf values were obtained and it became possible to prepare readily combined prophylactics containing tetanus toxoid with Lf values at least as high as 56 Lf/ml. with the TAB component totalling 5 × $10^9$ per ml.

Groups, each comprising approximately 30 individuals, were inoculated intradermally and subcutaneously with vaccines of different strengths and the antibody responses compared. With regard to the TAB component, it was found that 2 × 0·1 ml. of 5 × $10^9$ organisms/ml., injected intradermally, gave O-agglutinin responses and mouse passive protection against *Salmonella paratyphi* B challenge which were not significantly different from those obtained with subcutaneously injected 2 × 0·5 ml., or 0·5 and 1·0 ml. of 2·5 × $10^9$ organisms/ml. The route of injection did appear to affect the tetanus antitoxin levels for toxoids with the same Lf value, and with vaccines containing toxoid with an Lf value 22/ml. (2 × 0·1 ml.) injected intradermally the antitoxin levels were of the same order as those found with a subcutaneously injected vaccine (0·5 and 1·0 ml.) with an Lf value 11/ml.—a geometric mean titre in the region of 4 I.U./ml.

The intradermal method, as a result of these satisfactory trials, is now being adopted by the Army in the Home Commands for primary immunization against the enteric group of fevers and tetanus. The combined prophylactic contains 5 × $10^9$ organisms (*Salm. typhi* 2 × $10^9$ and *Salm. paratyphi A* and *B* 1·5 × $10^9$ each) in 1 ml. tetanus toxoid Lf20. 3 injections are given of 0·1 ml. each, the interval between the 1st and 2nd doses being 4 to 6 weeks and the third injection is given 6 to 12 months later. The results of this full-scale field trial will be awaited with interest but the experimental observations recorded in this paper suggest, with the preparation being employed, that the intradermal method has distinct advantages, with the already established advantage of reduced post-vaccinal reactions, over the previous method of immunization. It must be appreciated that the Vi-antigen of *Salm. typhi* is more or less inactivated by the methods employed for the preparation of the combined prophylactic.

*H. J. Bensted*

SHIH, P'eng-Ta. **The Use of Concentrated Typhoid Vaccine for Intradermal Immunization.** *Chinese Med. J.* Peking. 1958, July, v. 77, No. 1, 27–9.

The intradermal injection of TAB vaccine concentrated 10 times was compared with subcutaneous injection of the normal vaccine in a group of 1,391 students aged 12–18 years.

The intradermal group received 3 doses of 0·1 ml. at weekly intervals and the subcutaneous group 0·5 ml., 1·0 ml. and 1·0 ml. at weekly intervals.

General reactions were observed in 37 of 931 (3·97%) given intradermal injections and 34 of 460 (7·39%) given subcutaneous injections. The intradermal local reaction consists of the formation of a small vesicle, without any surrounding inflammation, which dries in 3–4 days and is followed by separation of the scab with no residual scar.

Such local reactions occurred in 22·3% of the intradermal group and they were noticeably less severe than in the subcutaneous group where 28·9% had local reactions.

There was no significant difference in the agglutinin titres produced by the 2 groups. *J. Nagington*

COLICHÓN, A., H. & ARANA SIALER, J. A. Estudio de la shigelosis en el Perú. **[Study of Shigellosis in Peru]** *Bol. Oficina Sanitaria Panamericana.* 1959, Mar., v. 46, No. 3, 227–35, 2 figs. [22 refs.]

The English summary appended to the paper is as follows:—

"A report is presented on a study of shigellosis in

Peru, carried out by modern methods in a special group of patients attended by private physicians and living in the best socio-economic conditions in the country. Approximately one case of shigellosis was found in every ten patients suffering from intestinal disturbances, and the majority of types of the four known pathogenic species of *Shigella* were observed to be present.

" The paper reiterates the conclusions of the study presented in 1942 and reports the finding of *Shigella boydii*—not referred to in the earlier study—as well as the presence of other types of *Sh. dysenteriae* and *Sh. flexneri* undetermined at that time, and presents the epidemiological evaluations derived from these findings.

" It is shown that *Sh. flexneri* increased in incidence from 1951 to 1957. Evidence is given of the presence in Peru of *Sh. boydii*, which follows *Sh. flexneri* in order of frequency; all types were encountered, type 1 being the most frequent.

" Data are presented on the occurrence of *Sh. flexneri* and *Sh. boydii* in different regions and provinces of Peru, as well as Lima. Findings are also reported on the pathogenesis in relation to age, and it is shown that there are numerous carriers of *Shigella* among adults.

" It is asserted that shigellosis always appears in outbreaks or waves which tend to become more accentuated during the summer season.

" Clinical and laboratory findings are described, and the paper concludes by affirming that the use of broad-spectrum antibiotics is less advisable in the case of chronic shigellosis because of alterations produced in the intestinal flora, superimposed or secondary infections, and the unfavourable effect of the antibiotics on the symbiotic action of intestinal flora."

RIERA ZUBILLAGA, A. *et al.* Diarreas y enteritis en el niño menor de dos años. [**Enteritis in Children under 2 Years Old**] *Archivos Venezolanos Puericult. y. Pediat.* 1958, Jan.–Feb., v. 21, No. 67, 15–38.

At the Central Hospital at Barquisimeto, Venezuela, during the period July 1, 1955, to June 30, 1956, 870 children under 2 years of age were admitted suffering from enteritis. 669 of them were treated as emergencies. More patients were admitted in November and December than in other months, which is in contrast with the generally accepted fact that in Venezuela most cases occur in May, June and July, though since the authors' figures are only for 1 year they admit no conclusions can be drawn. 60% of the severely ill patients were aged between 3 and 12 months, and 28% of all patients were not brought to hospital until the illness had lasted 5 days.

If children whose weight was not more than 15% below the average were considered as being in a satisfactory nutritional state, only 295 (33·9%) of the 870 could be so regarded. 209 patients had also some acute or subacute respiratory infection; 75 of these had bronchopneumonia; 8 each, pertussis, measles, or meningoencephalitis.

Treatment was on the usual lines as regards rehydration and diet, while the antibacterial drugs used were sulphadiazine 0·2 gm./kgm. body weight daily, usually combined with dihydrostreptomycin 0·5–1 gm. daily, chloramphenicol 50 mgm./kgm. daily, or oxytetracycline given in the same dose. All drugs were given orally; penicillin was given in addition to those suffering from extra-intestinal conditions as well.

Mortality. 104 (11·9%) of the total 870 patients died, 28 within 24 hours of admission, and 22 from causes other than enteritis. Only 12 of those who died were over 1 year old, and 26 less than 2 months old. As might be expected, those suffering from various degrees of malnutrition showed a much higher mortality than the rest. Out of the total 870 patients 82 had to remain in hospital for more than 15 days, though this was mainly because of other associated conditions, *e.g.* respiratory or other infections.

The authors suggest that the hospital needs more beds, doctors and nurses, and an improved laboratory service to enable the alkali reserve, electrolyte balance, etc., to be calculated more accurately, and they consider that other paediatric hospitals in the country should carry out similar investigations in order to ascertain the complete needs requisite for the treatment of infantile diarrhoea in Venezuela.

[Bacterial examination of the faeces of 115 patients was performed. *Shigella* species were isolated in 17, *Salmonella* species in 3, *Proteus* in 22, *Escherichia coli* in 25, and *Ps. pyocyanea* in 4, while 44 were negative, even though selective media were used.]

*W. K. Dunscombe*

TAKIKAWA, I. **Studies on Pathogenic Halophilic Bacteria.** *Yokohama Med. Bull.* 1958, Oct., v. 9, No. 5, 313–22, 7 figs.

In a considerable outbreak of gastro-enteritis observed in a hospital at Yokohama, a medium of high salt content was used for plating out the stools as it was expected that a staphylococcus might be responsible. This procedure led, however, to the isolation of a halophilic bacterium which had the characters of a *Pseudomonas* and appeared to have been conveyed to the patients in a dish of salted chopped cucumber.

In addition to diarrhoea, vomiting, nausea and moderate fever, the illness was peculiar for the rise of polymorphonuclear leucocytes in the blood.

Other similar strains were obtained from sporadic cases of diarrhoea but their incidence was low. The strains isolated at different times corresponded in being halophilic, with an optimum of 0·5 M (2·9%) of NaCl in the medium, liquefiers of gelatin, formers of indol and capable of fermenting many sugars without gas formation. They were straight Gram-negative rods with a terminal flagellum.

Among 11 student volunteers who swallowed undiluted culture or various dilutions of it, there was one who, after consuming 1 ml. of undiluted culture, developed sharp diarrhoea and vomiting of 3 days' duration, a temperature above 100°F. on the second day and considerable leucocytosis.

Observations on agglutination with the blood of patients were not particularly convincing.

The name *Pseudomonas enteritis* is proposed.

*J. W. McLeod*

## TUBERCULOSIS

CHEST & HEART ASS. **Chest and Heart Disease in the Commonwealth, 1958. The full transactions of the NAPT Commonwealth Chest Conference incorporating the Annual Conference of the British Tuberculosis Association,** London, 1–4 July, 1958. 443 pp., illustrated, 1959. London: Tavistock House North, Tavistock Square, W.C.1. [35s.; $6.00.]

> "Let Observation with extensive View
> Survey Mankind from China to Peru."

This couplet might well serve as the motto of the fifth Commonwealth Chest Conference, held in London in 1958 under the auspices of the National Association for the Prevention of Tuberculosis. The volume under review also contains the proceedings of the British Tuberculosis Association, which held its annual meeting at the same time. Some 1,500 delegates and many associates from all parts of the world were present.

There were 11 full and 6 sectional meetings of the National Association and 4 of the British Tuberculosis Association. Named speakers numbered approximately 160, to whom must be added members of the audience who took part in some of the discussions.

As stated in the foreword, NAPT conferences are mainly concerned with presenting a general picture of modern knowledge of chest disease, and the blend of social and medical viewpoints emphasizes that these diseases are a problem for the community as a whole in every part of the world and not the exclusive concern of health workers.

As usual in dealing with the transactions of such conferences it is impossible within reasonable space to do more than indicate the wide scope of the meetings. For example, the first topic discussed was *The World Anti-Tuberculosis Campaign, is it Succeeding?* (pp. 19–44). Speakers from Australia, WHO, South Africa, India, Scotland, Turkey, Ceylon, Pakistan, the United States and Canada all took part. In general the speakers were hopeful of success but eradication is still far distant. Tuberculosis infection is prevalent all over the world in a varying degree. In some African territories 2% of the population have been found to have open pulmonary tuberculosis and the best world estimate would be that ½–1% of all adults may be considered infectious. Much about tuberculosis remains unknown but there is a place somewhere for all known forms of tuberculosis control.

Another discussion of wide scope took place on the subject of *Tuberculosis and Leprosy—Resemblances and Divergences in Diagnosis and Treatment* (pp. 65–85). Speakers from England, Singapore, Nigeria, Kenya, Ghana and the United States took part. The discussion largely centred upon the question of immunity, particularly in relation to the antigenic resemblance between the leprosy and the tubercle bacillus. The opinion was expressed and supported that there is antagonism between the 2 diseases and relative crossed immunity between them. One speaker found evidence suggesting the possibility of a common antigen in tuberculin and lepromin but this was challenged. Research into the place of BCG vaccination in preventing leprosy was called for, and there was general agreement that tuberculosis and leprosy work should be combined.

The environmental aspects of respiratory disease, tuberculosis medical and social services in the British Commonwealth, lung cancer, mass radiography and BCG vaccination were other topics concerning which a great deal of valuable and interesting information was presented.

The audience at the meetings of the British Tuberculosis Association was entirely medical and therefore the proceedings were of more clinical interest than what has gone before.

The elimination of tuberculosis in Great Britain was discussed by 6 speakers who included in their review community surveys, selective mass radiography, serial tuberculin testing, BCG vaccination and the role of the industrial medical officer. The necessity or wisdom of compulsion in the carrying out of a community survey was discussed without any conclusion being reached.

The speakers on fungus disease, pneumoconiosis and sarcoidosis had much of interest to communicate. At the last session the subject of discussion was the trial in which the results of various operations for pulmonary tuberculosis were compared. This trial was initiated by the British Tuberculosis Association and 75 thoracic surgeons cooperated in it. The papers contain a great deal of detail but, as the Chairman remarked, all the information is contained in a book entitled *Major Surgery for Pulmonary Tuberculosis* by R. S. FRANCIS and M. P. CURWEN.

This volume is a rich mine of information about respiratory disease, especially tuberculosis, in which it is easy and profitable to dig. The familiar letters NAPT, which appear on the cover of the book, will not appear in future, as the National Association for the Prevention of Tuberculosis is now known as the Chest and Heart Association. It is greatly to be hoped that as the word "prevention" has disappeared from its title it will not also disappear from its thought and work.

*H. G. Calwell*

RILEY, F. **Tuberculosis in Hospital Nurses—Five Years Figures.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, Mar., v. 18, 38–45. [26 refs.]

Tuberculosis is accepted as an occupational hazard of nurses, and in the United Kingdom special rates of sickness insurance benefit may be paid to those whose claims are successful. It is not known what proportion of nurses contracting tuberculosis make claims for the special benefit but it is presumably high and analysis of successful claims should therefore present information on the incidence of the disease in nurses.

The present report is based on analysis of records of such claims by 1,116 nurses and assistant nurses, trained and student, employed in the hospitals of the National Health Service in England and Wales.

The annual number of cases of tuberculosis recorded was:

| Year | Number of cases | | | Population at risk (thousands) | | |
|---|---|---|---|---|---|---|
| | Total | Male | Female | Total | Male | Female |
| 1953 | 311 | 40 | 271 | 170·5 | 24·6 | 145·9 |
| 1954 | 281 | 44 | 237 | 174·3 | 24·7 | 149·6 |
| 1955 | 228 | 31 | 197 | 175·7 | 24·1 | 151·6 |
| 1956 | 166 | 37 | 129 | 180·2 | 23·8 | 156·4 |
| 1957 | 130 | 32 | 98 | 185·9 | 24·2 | 161·7 |
| Total | 1,116 | 184 | 932 | 886·6 | 121·4 | 765·2 |

It is thus seen that during the period of the survey the total number of female nurses at risk rose steadily and that of male nurses declined only a little. There was, however, a marked decline in the incidence of the disease in females whereas the male rate failed to decline, probably owing to the greater average age of the males and their longer stay in the service.

During the period under review there has been a decline of tuberculosis as recorded in these claims of some 60% compared with some 30% in notifications among the general population. Moreover the 1957 incidence among female nurses of 0·6 ± 0·1 per 1,000, is thought to be little different from that in the general female population although the nurses' group contains a relative preponderance of young adults of high susceptibility to infection.

Analysis of the distribution of cases by sex and age led to the conclusion that the relative incidence of tuberculosis at different ages resembles the pattern in the general population. The high incidence for males in the older age-groups is likely to be due to male nurses being on the whole older than females and to the fact that notification rates for older males in the population are generally higher than those for females. The morbidity rate was highest among nurses in mental hospitals (0·9/1,000) followed by 0·7 in tuberculosis, 0·6 in acute and 0·2 in chronic sick hospitals. Morbidity was by no means confined to the early years of service.

The inadequacy of the nurses' health service was demonstrated by the finding that X-ray records were available for only 542 of 802 nurses in the 1954–7 period; information about their tuberculin state was available for only 421. Of the 135 recorded as non-reactors 78 entered from 1950 onwards and 37 were given BCG. The time elapsing between BCG vaccination and the occurrence of tuberculous disease varied from 1 to 7 years with the greatest incidence in the third year.

The statistics produced reflect the general decline in tuberculosis coupled with the effectiveness of control and BCG programmes. Nevertheless the occupational hazard remains, for despite control the morbidity rate in nurses still approximates to that in the largely unprotected general population. *H. G. Calwell*

Fraser, J. W. **Significant Primary Pulmonary Tuberculosis in Young Contacts.** *Brit. J. Tuberculosis.* 1958, July, v. 52, No. 3, 255–63. [13 refs.]

This is a review of all children with a history of contact with tuberculous persons who were admitted to a Scottish hospital because of a significant radiological pulmonary abnormality attributed to tuberculous infection. The period covered was 1946–57 and the total number of children included was 154.

The age and sex distribution was:

| 0–4 | | 5–9 | | 10–15 | | Totals | |
|---|---|---|---|---|---|---|---|
| M | F | M | F | M | F | M | F |
| 42 | 28 | 21 | 22 | 15 | 26 | 78 | 76 |
| 45% | | 28% | | 27% | | | |

There was little variation in the total admissions of males and females.

The nature of the lesions seen in the initial skiagram is tabulated, and it is mentioned that practically all children with miliary and meningeal tuberculosis were admitted elsewhere so that few are included:

| Glands | | Collapse | | Effusion | | Post-primary | | Others | |
|---|---|---|---|---|---|---|---|---|---|
| M | F | M | F | M | F | M | F | M | F |
| 19 | 21 | 42 | 31 | 5 | 3 | 2 | 10 | 10 | 11 |
| 26% | | 48% | | 5% | | 8% | | 13% | |

Post-primary lesions occurred in the 11–14-years age-group (females 10 and males 2).

Parents were the chief source of infection; mothers infected 52 children (34%), fathers 41 (26%), brothers 9 (6%), sisters 26 (17%) and other persons, mostly relations, 26 (17%). Very few sources of infection were found among unrelated persons.

The sputum state of the source cases is given: positive 112, negative 10. The bacilli were found on direct examination in all but 3; these yielded positive cultures. 31 patients who died of advanced pulmonary tuberculosis and for whom the results of bacteriological examination were not available were considered to have had positive sputa. Only 3 sputa gave negative cultures and these were probably poor specimens.

The interval between notification of the source case and the discovery of the condition in the child was:

| | Months | | |
|---|---|---|---|
| | 1–3 | 3–6 | over 6 |
| Contacts with symptoms and X-ray changes .. .. .. | 44 | 13 | 23 |
| Contacts without symptoms but with X-ray changes .. .. | 38 | 2 | 16 |
| Contacts who were themselves index cases .. .. .. | | 18 | |

The majority of children with active primary lesions were X-rayed within 6 months of notification of the source case.

Of the 12 children with post-primary tuberculosis all had moderately advanced disease and all had positive sputa except one whose gastric residue yielded a positive culture.

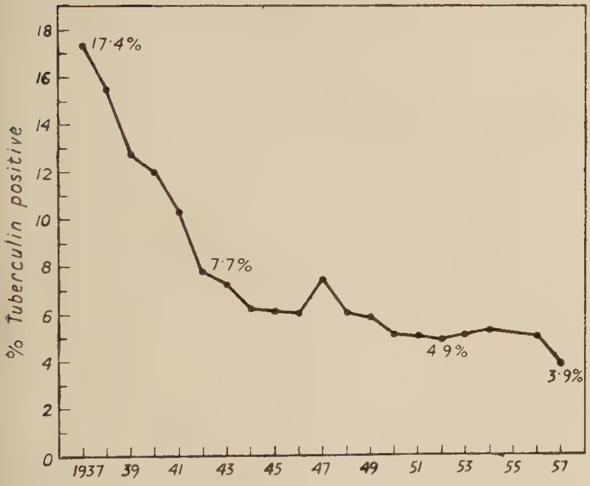
It was not possible to determine accurately the duration of infectivity of the source cases but it was estimated that they were expectorating tubercle bacilli for at least 3 months before diagnosis. To this period must be added a period of some 8 weeks' delay in isolating the source case.

The preponderance of children in the youngest age-group and the risk to girls in the 10–15-years group are emphasized. The finding that 17% of the source cases were outside the immediate family circle shows the importance of examining even the most casual child visitor to infectious households.

Reactor contact children under the age of puberty should be X-rayed initially and again in 3 months. In the absence of any significant abnormality no further X-ray examination would be required. Children aged 10–15 require special supervision. *H. G. Calwell*

Bojlen, K. Tuberkulose undersögelser i et skolemilieu. **[Tuberculosis Investigations in a School Environment]** *Ugeskr. f. Laeger.* 1959, April 2, v. 121, No. 14, 548–553. 10 tables, 1 chart, 10 refs.

This investigation concerns the schools of Copenhagen during the period 1937–57, and a chart gives the percentages of spontaneous positive tuberculin reactions among the scholars in their first school year. It is an index to the degree of infection to which the children of Copenhagen are exposed during the first 7 years of their lives. It starts in 1937 with 17·4%. By 1942 the fall has been so rapid that it is down to 7·7%. This fall may be traced to (1) the establishment of a central station for combating tuberculosis in 1935, (2) the compulsory provision in 1935 of raw milk and cream from tuberculosis-free herds, and (3) an extension of this measure in 1938. Between 1942 and 1952 the fall flattens out, with a short upward jerk probably due to an error of recording. In 1957 the fall has again become rapid, ending at the record low level of 3·9%. This may well reflect the fact that in 1950 a maternity centre in Copenhagen took to providing BCG vaccination for all its newborn infants.



The Danish law of 1946 provides for the annual tuberculosis control not only of every schoolchild, but also of school staff. Between 1944 and 1957 active pulmonary tuberculosis was discovered in 50 members of the school staff. Bojlen's many tables deal with such matters as the incidence of tuberculosis in the school staff from year to year, the finding of tubercle bacilli on gastric lavage of schoolchildren from 1951 to 1957, the BCG vaccinations from 1949 to 1958, the number of invertors from 1937 to 1957 among scholars on entering school in 1937, and the finding of tubercle bacilli among invertors and the subjects of BCG vaccination. His main appeal is for earlier and more systematic BCG vaccination of schoolchildren, and he gives a friendly pat on the back of the members of that maternity centre which had the courage to submit all its babies to BCG vaccination in 1950.

*Claude Lillingston*

Ashworth, T. G. & Van Der Walt, E. D. **A Transkei Mission Hospital Practice: Incidence of Disease with special reference to Tuberculosis.** *South African Med. J.* 1958, Aug. 23, v. 32, No. 34, 849–53.

The hospital where this work was done is in the Cape Province of South Africa and serves an exclusively Bantu population of the Xhosa tribe. The people are agricultural and pastoral but some of the men migrate to the gold mines to work. Maize is the main crop and the cows give a very poor milk supply so that malnutrition is prevalent. Hygiene is unknown and indiscriminate defaecation and spitting are common.

During the period July 1957 to January 1958, 2,002 patients attended the hospital, of whom 682 (34·1%) were admitted. Their age distribution was:

| Years | Males | Females | Total |
|---|---|---|---|
| 0–5 .. .. .. | 402 | 384 | 786 |
| 6–29 .. .. .. | 197 | 291 | 488 |
| 30 and over .. .. | 270 | 458 | 728 |
| Total .. .. .. | 869 | 1,133 | 2,002 |

The list of diseases seen is headed by tuberculosis; there were 394 patients in whom tuberculosis was diagnosed for the first time and 69 return cases of tuberculosis. 245 patients with tuberculosis were admitted for treatment. Details of the new cases were:

| | Age | | | |
|---|---|---|---|---|
| | 0–5 | 6–29 | 30 and over | Total |
| Pulmonary and cervical adenitis .. .. .. | 118 | 60 | 165 | 343 |
| Peritonitis .. .. .. | — | 4 | 6 | 10 |
| Meningitis .. .. .. | 5 | 2 | 3 | 10 |
| Spine .. .. .. | 6 | 2 | 2 | 10 |
| Hip and Knee .. .. | — | 1 | 8 | 9 |
| Pericarditis .. .. | — | 3 | 5 | 8 |
| Liver and Spleen .. | — | — | 4 | 4 |
| | 129 | 71 | 194 | 394 |

The highest incidence was in young children and in the age-group over 30 years. The pulmonary form of the disease was present in 87%. The discovery rate of 19·6% in the 2,002 out-patients indicates the serious tuberculosis situation in the region.

All those classified as having pulmonary tuberculosis were X-rayed except a few infants. Clinical diagnosis was sufficient in the majority. Some of the men who had been away working in the gold mines had silicosis by itself or combined with tuberculosis. Carcinoma of the bronchus may have been missed but the authors do not believe that it occurs frequently.

The tuberculin test was used routinely in children under 2 but only in a few cases was it the exclusive basis of diagnosis. The diagnosis of meningitis was made on clinical grounds and the findings in the cerebrospinal fluid.

It was possible to admit only the most acute cases. The other patients were asked to attend a streptomycin clinic twice weekly or if they lived too far away they were given a 3 months' supply of isoniazid. PAS was rarely used. Attendance was very unsatisfactory.

*H. G. Calwell*

Custer, E. W. **A Pilot Study of the Tuberculin Test for Case Finding in a General Hospital.** *Amer. Rev. Tuberculosis.* 1959, Mar., v. 79, No. 3, 378–81, 1 fig.

St. Joseph's Hospital, South Bend, Indiana, deals with patients from an area where the newly reported cases of tuberculosis amount to 29·3 per 100,000 and the mortality 4·9 per 100,000.

Of the 3,800 patients admitted between May and October 1957, 2,484 (64%) completed a Mantoux test with PPD-S (0·001 mgm. = 5 TU). Reasons for failure to complete the test in the remainder are given.

20% had a weak response (5–10 mm.), 35% had a reaction of 10–20 mm., 30% more than 20 mm., and severe in 13%. The total number of positive reactions was 603 (24·3%) reaching 44% in the age-group 45–54. In older age-groups the percentage dropped both qualitatively and quantitatively. In most groups the positive incidence was about 10% higher in males than females.

Owing to administrative difficulties it is thought that in spite of the reduction in cost, the use of a tuberculin test followed by an X-ray in positive cases is not a practical method of excluding tuberculosis in patients where there is a quick turnover. Details of the investigation are given in tables and a graph.

*F. H. Young*

Cheung, O. T. **A Comparison of Mantoux and Heaf Tuberculin Tests.** *Canadian J. Pub. Health.* 1959, Mar., v. 50, No. 3, 117–19.

This study was made in a tuberculosis hospital in Canada. The group of 400 patients on whom the tests were done consisted of 245 males and 155 females, of whom 48% were aged 20–39 years and 38% 40–69 years.

A Heaf test with PPD (2 mgm./ml.) was done on the right forearm and read daily for 5 days wherever possible; a Mantoux test with 5 TU of OT was done on the left forearm at the same time. If the 5 TU Mantoux test was negative at 72 hours it was repeated with 100 TU. All tests were done and read by the author. The criteria of a positive Heaf reaction were those of Heaf, and the criterion of a positive Mantoux reaction was induration of 6 mm. or more.

There were 10 patients who failed to react to all tests; none showed evidence of tuberculosis and were not retained for treatment. Of 16 patients who failed to react to 5 TU but reacted to 100 TU 13 were Heaf-negative and 3 Heaf-positive. The Heaf test in this series was very slightly more sensitive than the Mantoux with 5 TU. Among the 13 patients who did not react to 5 TU and Heaf but reacted to 100 TU, 4 had bacteriological or histological proof of tuberculosis. This shows that neither the 5 TU Mantoux nor the Heaf test is sufficient to eliminate the possibility of tuberculosis.

There were 374 patients who reacted to 5 TU and to the Heaf test. In 14 of these the Heaf test was found to be more easily read than the Mantoux, the reactions being more distinctly positive. It was concluded that the sensitivity of the Heaf test lies between the 5 TU and the 100 TU Mantoux tests.

The degree of reaction to the tests was compared:

| Heaf Reaction | | 5 TU Mantoux<br>Diameter of induration in mm. | | | | |
|---|---|---|---|---|---|---|
| Grade | Number | Neg. | 6–10 | 11–15 | 16–20 | over 20 |
| 0 | 23 | 23 | – | – | – | – |
| I | 86 | 3 | 23 | 40 | 19 | 1 |
| II | 21 | – | 1 | 10 | 8 | 2 |
| III | 232 | – | 6 | 98 | 109 | 19 |
| IV | 38 | – | – | 3 | 20 | 15 |
| Total | 400 | 26 | 30 | 151 | 156 | 37 |

These results show a direct correlation between the degree of the reaction to the 5 TU Mantoux and Heaf tests.

The findings of the study suggested that the third day is suitable for reading the Heaf test. No patients who showed a negative Heaf reaction on the 3rd day showed a positive reaction later. 1·9% of those positive to Heaf and Mantoux 5 TU tests on the third day showed such faint reactions on the fifth day that they could not be called positive.

*H. G. Calwell*

O'Grady, F. **Erythema Component of the Primary Mantoux Response.** *Brit. J. Dis. Chest.* 1959, Apr., v. 53, No. 2, 181–6, 1 fig.

It is taught that erythema by itself should not be considered a criterion of a positive Mantoux reaction. The occurrence of erythema without induration is, however, not rare, and O'Grady has studied it as a component of the primary Mantoux reaction—that is to say the reaction in subjects who have either never been tested before or who have not been tested for at least 3 months.

The subjects tested fell into 3 groups:

1. 134 non-tuberculous subjects.

2. and 3. Patients suffering from active tuberculosis, subdivided according to the pattern of their Mantoux reaction.

2. 138 tuberculous patients giving "normal" reactions.

3. 82 tuberculous patients giving "tuberculous" reactions.

[O'Grady's definition of "normal" and "tuberculous" in this context was given in a previous paper (this *Bulletin*, 1956, v. 31, 899). Patients with active tuberculosis gave Mantoux reactions, the majority of which were characterized by extreme transience of definite or shallow induration. In addition the whole response tended to be of shorter duration.]

In a typical positive response 2 zones of erythema appear, reddening of the indurated plaque and reddening of the area beyond it. It was seen that there was an overall but not close correlation between the peak size of induration and the peak size of erythema in all 3 groups. Generally the average peak size of erythema increased with the peak size of induration.

The relation between peak size of induration and the day of maximum erythema was examined. The 3 groups were very similar and in each the average time to peak erythema was later in those with larger reactions.

No essential differences were seen in the form of the erythema component between "normal" and "tuberculous" reactions but there was a small difference in the relative duration of erythema and induration between the groups. It was found that in both the groups giving "normal" responses erythema outlasted induration in about 10% of subjects whereas it outlasted induration both more frequently and for longer periods in those giving "tuberculous" reactions.

The erythema component of negative reactions was studied. The negative reactions were of 2 kinds, *viz.* reactions to ineffective doses of tuberculin with subsequent positive reaction to larger doses and reactions in patients who failed to react to 100 TU. In both groups the majority of patients who failed to react with induration gave no erythematous response. In those who reacted with some induration erythema always developed, and outlying erythema occurred in one-half of the patients in each group. There was no essential difference in the form of the erythema response between these and "normal" reactions.

The findings are discussed. There was no evidence that a particular form of erythema response occurred in the presence of active tuberculosis but florid erythema appeared to be more common in patients with active disease. O'Grady suggests that the non-specificity of erythema has been over-emphasized.

*H. G. Calwell*

O'Grady, F. **Changes in Erythema as the Index of Sensitisation and Activation.** *Brit. J. Dis. Chest.* 1959, Apr., v. 53, No. 2, 187–92. [13 refs.]

Sensitization in the context of this study was defined as being present when the reaction to a second dose of tuberculin was 30% greater than that to the first dose. The response to both doses was recorded in terms of induration and total and outlying erythema. Increases of 30% in each of these responses was identified as induration sensitization, total erythema sensitization and outlying sensitization.

The patients studied were divided into 3 groups: (a) those positive to 1 TU. These were re-inoculated with 1 TU at intervals of 1–15 days. This group consisted of 22 non-tuberculous and 58 tuberculous patients of whom 15 gave "tuberculous" responses. (b) Patients negative to 1 TU but positive to 10 TU. These were re-inoculated at intervals of 1–15 days with 1 TU. This group consisted of 43 non-tuberculous patients and 93 tuberculous patients of whom 46 gave "tuberculous" responses. (c) Patients negative to 1 and 10 TU but positive to 100 TU. These were re-inoculated at 2–3-day intervals with 10 TU and after a further 2–3 days with 1 TU. This group contained 8 non-tuberculous and 17 tuberculous patients.

No evidence was found to support the view that patients can be divided into those who regularly fail to produce any erythema and those who produce florid erythema.

There was some correlation between changes in induration and total erythema in that 9 of 11 patients showing increased induration showed increased total erythema, and all patients showing decreased induration showed decreased erythema.

Induration sensitization was found in 7/22 non-tuberculous patients and 5/58 tuberculous patients. Both total and outlying erythema sensitization were found in 11 patients in each group. Induration sensitization was found only in combination with outlying erythema sensitization and then only in 2 tuberculous patients.

Comparisons between induration and outlying erythema in patients positive to 10 TU showed that the results for total erythema were identical except that 2 patients who showed no change in induration or outlying erythema showed a 30% increase in total erythema.

The comparative efficiency of changes in induration and erythema as means of distinguishing between active and inactive tuberculosis in patients positive to 10 TU was studied. Of the non-tuberculous patients 82% showed induration sensitization, 62% total erythema sensitization and 48% outlying erythema sensitization. Induration sensitization occurred together with total erythema sensitization in 55%, together with outlying sensitization in 39% of the non-tuberculous patients.

In the corresponding patients with active tuberculosis 30% showed induration sensitization, 40% total erythema sensitization and 31% outlying erythema sensitization. Induration sensitization was found together with total erythema sensitization in 17% and together with outlying erythema in 15% of tuberculous patients. "The best that can be said for sensitization as a diagnostic test is that the development of both induration and erythema sensitisation in the presence of active tuberculosis is uncommon."

*H. G. Calwell*

Mestitz, P. & Pollard, A. C. **The Diagnosis of Tuberculous Pleural Effusion.** *Brit. J. Dis. Chest.* 1959, Jan., v. 53, No. 1, 86–94, 1 fig. [Numerous refs.]

The authors have collected data on many series of cases of pleural effusions in which the diagnosis of tuberculosis as the cause has been made by various methods. The figures are remarkable for the variations of success which are reported by the different authors. This paper considers 112 cases of pleural effusion and examines a number of indirect aids to ascertain which if any are of value in diagnosis.

Clinical presentation is shown to be of little practical value in diagnosis.

A positive Mantoux was found in all cases with a proven tuberculous aetiology. The erythrocyte sedimentation rate was found to be of no value. A high percentage of lymphocytes was found in 65 out of 68 tuberculous pleural fluids examined. Smear examination of pleural fluid seldom yielded tubercle bacilli. The authors obtained 28·6% of success by cultures. In the series of 112 patients the diagnosis was in 97 by biopsy and 22 by other means, and this is by far the most valuable method. A positive Mantoux test and a predominantly lymphocytic fluid indicate a presumptive diagnosis. *F. H. Young*

HULSE, W. F. **Laryngeal Tuberculosis.** *Brit. J. Dis. Chest.* 1959, Jan., v. 53, No. 1, 75–85, 1 fig.

The author commenced this paper by a short account of the clinical features of laryngeal tuberculosis, but his contention that the laryngeal disease is *always* a complication of *severe* pulmonary tuberculosis will not be accepted by many workers.

A table is given showing that in Cutahoga county, Ohio, the occurrence of laryngeal tuberculosis and the associated death-rate has fallen dramatically since antimicrobial drugs have been used. He discusses the use of these drugs and their toxic effects.

The paper does not add anything to what is already generally known about this condition. *F. H. Young*

BREATHNACH, C. S. **The Conservative Treatment of Primary Tuberculosis in Children. A Five-Year Follow-Up.** *Brit. J. Tuberculosis.* 1958, Oct., v. 52, No. 4, 330–37. [28 refs.]

In 1951, 465 children under 15 years of age suffering from primary tuberculosis came to the Primary Tuberculosis Clinic, Dublin, for the first time.

281 of these were reviewed in 1957, giving a minimum follow-up of 5 years. 43 had calcified primary tuberculosis, the remainder were diagnosed as having active disease, of whom 147 had a primary complex, 23 a primary focus only, 74 glandular enlargement only, and 15 with bilateral enlargement. The number of active cases treated institutionally and at home was approximately equal; 11 had chemotherapy.

Pulmonary complications arose in 102 patients, all originally pulmonary primaries. Of these 52 developed extensive glandular enlargement, in 46 segmental lesions and in 15 pleural effusion appeared. No miliary tuberculosis or cavitation of a primary focus occurred. 82·7% of marked glandular enlargement cases were in children under 6 years of age, 75% of all segmental lesions were in children under 6 years of age, 18 children had incomplete re-expansion, and 6 children developed meningitis or skeletal tuberculosis, of whom 4 died. All deaths occurred in children of under 5 years of age. Treatment was almost exclusively conservative. This gave a mortality of 5% in children under 2, and 2% in children under 5 years of age. *F. H. Young*

SMART, J. & GOUGH, J. **The Treatment of Pulmonary Tuberculosis with Prolonged Streptomycin, Sodium P-Aminosalicylate and Isoniazid.** *Brit J. Tuberculosis.* 1958, July, v. 52, No. 3, 238–43. [17 refs.]

The authors point out that although reports on the results of chemotherapy carried out for long periods are common, few have yet appeared in which the follow-up period covered years.

They report the results on 75 patients (60 additional cases had to be omitted for one reason or another). The follow-up period averaged 1 to 2 years with extremes of 6 months and over 3 years. All three standard drugs were given simultaneously in the normal dosage. 38 patients had advanced disease, 62 had a pre-treatment positive sputum, and 53 had definite cavitation. The period of drug treatment varied from 1 to 3 years with an average of about 20 months.

69 (92%) were classified as satisfactory; 1 died of cor pulmonale with disease still active.

2 patients still have a positive sputum, 3 who have thin walled cavities with a negative sputum may be satisfactory. No patient classified as satisfactory on completion of treatment has relapsed.

Of patients with bacilli initially sensitive, 2 patients became fully resistant to streptomycin and isoniazid, 1 after 6 and 36 months' therapy, and 1 patient became partially resistant to PAS after 12 months.

This is a useful paper having the advantage of being the observations of a single worker, though this limits the number of cases available for consideration. *F. H. Young*

JEKER, K., LAUENER, H., REGLI, J. & FRIEDRICH, T. **The Tolerability of Calcium Benzoyl-PAS and Calcium PAS. A Double Blind Study.** *Amer. Rev. Tuberculosis.* 1959, Mar., v. 79, No. 3, 351–6, 1 fig. [15 refs.]

In view of the divergent views on the lack of toxic symptoms, mainly gastro-intestinal, produced by calcium B-PAS [this *Bulletin*, 1956, v. 31, 20; 1957, v. 32, 744], it was decided to carry out a double blind trial. The use of calcium PAS was compared with PAS on 70 assessable patients who were treated with calcium B-PAS and compared with 80 treated with PAS. Satisfactory precautions appear to have been taken to make trial comparable from all points of view except that there was a greater excess of female patients in the PAS group.

Cachets containing 1·25 gm. of calcium B-PAS (= 1 gm. acid B-PAS) with 25 mgm. of isoniazid, and 1·31 gm. of calcium PAS (= 1 gm. acid PAS) with 25 mgm. of isoniazid, respectively, were given to each group. For a period of 12 weeks 4 cachets were given twice daily to patients weighing up to 50 kgm., 3 times a day to those weighing 50–70 kgm., and 4 times a day to those weighing over 70 kgm.

If either preparation was badly tolerated the daily dose was reduced to 8 gm. daily, and if this had no effect a change over to the other preparation was made. If the patient was intolerant to both, PAS therapy was stopped. 175 patients started the test, 85 with calcium

B-PAS, and 90 with PAS. After rejection of 15 in the B-PAS group, and 10 in the PAS group for various reasons, 70 of the B-PAS, and 80 of the PAS were available for assessment. 63 (90%) of the B-PAS group and 50 (63%) of the PAS group completed the 12-week trial. 7 (10%) of the B-PAS group and 30 (37%) of PAS group had symptoms sufficiently severe to cause cessation of the treatment.

Complete lack of toxic symptoms occurred in 51 (73%) of the B-PAS group, against 35 (44%) of the PAS cases.

Owing to intolerance B-PAS was substituted for PAS in 21 patients, and in 2 the reverse. Of the 21, 16 completed treatment, 12 without any symptoms. Of the 2 in which PAS had to be substituted for B-PAS, 1 completed treatment. Allergic symptoms were common in the PAS group. It was thought that it was justified to carry out the trial for 12 weeks only as symptoms of intolerance usually occurred within this period. *F. H. Young*

Eloy, L. M. Traitement de la tuberculose pulmonaire par le p-aminosalicylate d'isoniazide. **[Treatment of Pulmonary Tuberculosis with Dipasic]** *Ann. Soc. Belge de Méd. Trop.* 1958, Oct. 31, v. 38, No. 5, 1011–15.

The author has treated 19 sputum positive patients with "Dipasic" for 1–2 months, 9 of whom were thought to have organisms resistant to the 3 standard drugs. He considers that the results have been better than would be expected, and no complications occurred. He does not mention what is considered in England to be the disadvantage of this drug—the development of isoniazid resistance. It is only a preliminary note. *F. H. Young*

East Africa. **Comparative Trial of Isoniazid in combination with Sulphone or PAS in the Treatment of Acute Pulmonary Tuberculosis in East Africans. A Co-Operative Investigation in East African Hospitals and Laboratories with the Collaboration of the British Medical Research Council.** *Tubercle.* 1959, Feb., v. 40, No. 1, 1–3. [17 refs.]

The comparative trials of anti-tuberculous drugs carried out under the auspices of the British Medical Research Council have received world-wide acceptance; and this trial has been carried out in a similar manner. The results can therefore be considered as reliable.

Circumstances in East Africa made the usual combination of drugs inapplicable; so it was decided to try the effects of isoniazid 200 mgm. daily with diaminodiphenylsulphone 100 mgm. daily in 1 dose (DH series) against treatment by a standard regime of isoniazid 200 mgm. daily and PAS (sodium salt) 10 gm. daily in 2 doses (10PH).

From 19 March 1956 to October 1956, 75 patients were allocated treatment with the DH regime, and 71 with the 10PH regime. Certain exclusions had to be made subsequently and finally 61 of the DH and 56 of 10PH patients were available for consideration. The bacteriological results were considered most important. At the end of 3 months 66% of the DH and 81% of 10PH group had negative smears; at the conclusion of the 6 months' trial the figures were 71% and 96%, respectively.

The culture results followed a similar pattern; at the end of 6 months the negative cultures were obtained in 58% of the DH, and 90% of the 10PH groups.

Sensitivity tests showed that at the end of 6 months 17 out of 18 of the positive cultures in the DH group were isoniazid resistant against 3 out of 5 of the 10PH group. 11 of the former were completely resistant compared with none in the latter. 4 patients had cultures resistant to PAS but there was some doubt whether in some the resistance had developed during treatment. No definite evidence of DDS resistance was obtained. The clinical and radiological improvement in the 2 groups did not show a statistically significant difference.

It is concluded that the addition of DDS to isoniazid in treatment has had little effect from the point of view of the reduction of resistance and sputum conversion. Whether it had a more favourable clinical and radiological effect than isoniazid alone will be decided by a further trial which is in progress at present. *F. H. Young*

Viallier, J. & Cayré, R. M. Sur l'activité antituberculeuse *in vitro* du sel de dihydrostreptomycine du sulfoniazide (streptorilone). **[The Antituberculous Activity *in vitro* of the Dihydrostreptomycin Salt of Sulphoniazid (Streptorilone)]** *C.R. Soc. Biol.* 1958, v. 152, No. 11, 1501–3.

The determination of the minimum inhibitory concentration of Streptorilone [the dihydrostreptomycin salt of sulphoniazid] for 10 freshly isolated strains of tubercle bacilli shows that the sensitivity for this salt is equivalent to the dihydrostreptomycin or isoniazid sensitivity of the particular strain.

Similar determinations made on the serum of patients undergoing treatment with Streptorilone showed that none of the sera inhibited the growth of a strain resistant to both isoniazid and streptomycin although they inhibited bacilli sensitive to one or other, or both of the drugs. *S. R. M. Bushby*

Doy, C. H., Dixson, Shirley & Rubbo, S. D. **Chemotherapy of Tuberculosis. IV. Stability of Hydrazones of Isoniazid in Biologic Fluids.** *Amer. Rev. Tuberculosis.* 1959, Apr., v. 79, No. 4, 492–6, 1 fig. [12 refs.]

"The stability of three hydrazones of isoniazid, which have been investigated clinically, has now been studied in various biologic materials. Particular attention has been given to the stability of Verazide in blood and serum.

"The results show that the hydrazones, Verazide, Phtivazid, Nupasal-213 (or Salizid) are broken down rapidly in serum, whole blood, and tissue homogenates. The breakdown is probably hydrolytic in nature, protein dependent, and yields isoniazid and some *iso*nicotinic acid. It is suggested that these hydrazones owe their *in vivo* activity to the liberation of chemotherapeutically active isoniazid."

Haber, E. & Osborne, R. K. **Icterus and Febrile Reactions in Response to Isonicotinic Acid Hydrazine. Report of Two Cases and Review of the Literature.** *New England J. of Med.* 1959, Feb. 26, v. 260, No. 9, 417–20, 2 figs. [20 refs.]

Pointing out that only 2 fully documented cases of icterus, and 10 of drug fever, have been published the authors report 2 further cases in considerable detail. Both symptoms disappeared when the isoniazid was withdrawn, and in 1 both recurred when isoniazid was given again; in the other the fever recurred and liver function tests were abnormal, but icterus was not noted presumably because only 1 test dose of 100 mgm. was given. Both patients had hypersensitive reactions to PAS. A summary of the features of the cases previously described is given and it is interesting to note that in 50% PAS sensitivity was reported. A list of references is given. *F. H. Young*

Merritt, A. D. & Fetter, B. F. **Toxic Hepatic Necrosis (Hepatitis) due to Isoniazid: Report of a Case with Cirrhosis and Death due to Hemorrhage from Esophageal Varices.** *Ann. Intern. Med.* 1959, Mar., v. 50, No. 3, 804–10, 2 figs. [11 refs.]

"A case is presented of hepatic cirrhosis and death from bleeding esophageal varices believed to be secondary to administration of isoniazid. Though the patient had received para-aminosalicylic acid during her initial therapy, and subsequently was shown to have a febrile response to a single oral dose, there was no evidence of hepatocellular damage from this drug.

"Hyposensitization to isoniazid was accomplished without complications."

Macleod, H. M., Hay, D. & Stewart, Sheila M. **The Use of Pyrazinamide Plus Isoniazid in the Treatment of Pulmonary Tuberculosis.** *Tubercle.* 1959, Feb., v. 40, No. 1, 14–20.

The efficacy of pyrazinamide against tubercle bacilli seems to be proved but reports on its toxicity have prevented its extensive use. It is normally used in combination with isoniazid, and it is alleged that it is as efficient when the bacilli are partially resistant to the latter.

11 patients are reported on in a trial to determine the truth of this allegation. 2 had had no treatment with isoniazid and their organisms were fully sensitive; in 5 the organisms were resistant to 0·2 to 1·0 μgm. per ml., and in 3, to 5 to 50 μgm. per ml. 1 had a varying resistance. All patients had bacilli resistant to PAS and streptomycin.

Pyrazinamide was given in doses of 40 mgm. per kgm. body weight in 2 doses daily, and isoniazid 200 mgm. to the 2 sensitive cases and 3 resistant cases; the remainder received 600 mgm. daily with pyridoxine.

The period of treatment varied from 3 to 24 months (1 patient who was thought to be developing toxicity stopped treatment after 2 months and is omitted).

Bacteriologically the 2 sensitive patients and 1 with partial resistance converted and remained so. 1 patient with varying resistance had a transient conversion. Of the other 6, one-half with partial and one-half with resistant organisms, 2 had transient conversion and 4 remained positive. The radiological improvement was not very dramatic.

The danger of toxicity as reported in the literature is reviewed.

The results are not impressive and the author concludes that the main use of the therapy is as a short term cover for operations. *F. H. Young*

De Leon, A. R. & Lopez, A. B. **Cycloserine in the Treatment of Advanced Pulmonary Tuberculosis.** *J. Philippine Med. Ass.* 1958, Dec., v. 34, No. 12, 721–8, 4 figs. on 2 pls.

This is a report on 20 patients treated with cycloserine 0·5 gm. daily, and isoniazid 4·0 mgm. per kgm. body weight, for approximately 6 months. In 1 patient, treatment had to be abandoned because of toxic reactions. In the others the toxic manifestations were mild and not permanent. Because of failure to respond to other drugs it was assumed that resistance was present. Radiological improvement was marked or moderate in 8 patients and slight in 6. The small number of patients treated and lack of full laboratory investigation detracts from the value of the paper. 4 case histories are given. *F. H. Young*

Weinstein, H. J. & Koler, J. J. **Adrenocorticosteroids in the Treatment of Tuberculosis.** *New England J. of Med.* 1959, Feb. 26, v. 260, No. 9, 412–17, 2 figs.

In view of the conflicting reports on the value of adrenocorticosteroids in treating patients suffering from pulmonary tuberculosis, an investigation of its use was undertaken on 49 patients compared with 51 carefully matched patients retained as controls. All were treated with isoniazid 300 mgm. and PAS or one of its salts 9–12 gm. daily. The study group received prednisolone for 68 days starting with 20 mgm. daily and gradually reduced doses.

6 patients (4 of the study group) were withdrawn for various reasons. These were replaced by new admissions. The period of observation ranges from 6 to 16 months.

3 patients died; 2 from the study group, one of coronary occlusion, and the other from pulmonary insufficiency and haemorrhage. The patient from the control group died of pyrazinoic acid amide toxicity. No specific ill effects from the steroid were noted.

The results were favourable in the following respects.

Sputum conversion occurred earlier, though finally the difference was slight. Cavity closure was also favourable: only 1 of the treated group is still in hospital with cavitated disease against 9 of the control group. Excellent X-ray clearing was much commoner in the treated group, especially in far advanced patients.

The authors consider that the period of hospital treatment was appreciably reduced in the treatment group without corresponding disadvantage, and increased cavity closure occurred. *F. H. Young*

Turner, P. P. **The Effects of Prednisolone on Chronic Drug Resistant Pulmonary Tuberculosis in Kenya Africans.** *Brit. J. Dis. Chest.* 1959, Jan., v. 53, No. 1, 95–8, 2 figs. on pl. [15 refs.]

"Nine patients with chronic, drug resistant, pulmonary tuberculosis were given prednisolone in addition to INAH and PAS. All showed rapid and considerable clinical improvement. One showed marked radiological clearing and one regained her sensitivity to streptomycin and became culture negative after further treatment. None became sputum negative as a result of the addition of the prednisolone. It is concluded that prednisolone has a definite place in the treatment of chronic pulmonary tuberculosis, even if the covering chemotherapy is not fully effective because of drug resistance."

Nodine, J. H., Yoshizawa, H., Weiss, W., Stein, S. C., Guth, Rachael & Tummillio, Mary. **The Effect of L-Triiodothyronine in Pulmonary Tuberculosis: A Pilot Study.** *Amer. J. Med. Sci.* 1959, Jan., v. 237, No. 1, 27–41, 5 figs. [17 refs.]

For many years occasional papers have appeared in the literature suggesting that in patients with hyperthyroidism tuberculosis pursues a favourable course, but when thyroid extract has been administered the results have been very equivocal. Recently Lurie [this *Bulletin*, 1956, v. 31, 945] has published results in experimental animals showing a favourable response to triiodothyronine. This paper details the results of its use on 29 patients with carefully paired controls. Starting with a daily dose of 50 to 100 mgm. of the drug this was increased by 25 mgm. every 2 weeks until evidence of mild hyperthyroidism was found. An additional 7 patients were treated but their pairing with 10 controls was not thought to be entirely satisfactory. Interesting observation in the Endocrine Department showed that the treated group failed to show the increase in serum cholesterol which appeared in the control group, presumably as the result of general improvement in health. In addition the rapid 1-131 uptake was suppressed.

24 patients were observed for 3, and 18 for 6 months, but by none of the criteria used was there any evidence that benefit was received compared with the controls. The authors suggest that the percentage of those patients with acute infiltrative type of disease was high, so these results do not exclude the possibility that benefit might be received by selected patients of the highly resistant type.

This is an admirable paper in which the greatest care was taken to ensure a fair comparison between treated and control groups. *F. H. Young*

Arblaster, P. G., McWhinney, I. R., Smith, R. A. & Cross, K. W. **Medical Treatment as an Alternative to Thoracoplasty in Pulmonary Tuberculosis.** *Thorax.* 1959, Mar., v. 14, No. 1, 14–20, 1 fig.

Since the widespread use of antimicrobial drugs surgical treatment of tuberculosis, especially thoracoplasty, has become increasingly less popular, but little information is available to determine how patients who were suitable for thoracoplasty fared if instead of the thoracoplasty long-term medical treatment with drugs was used. From the records of South Warwickshire, 259 patients out of the 1,183 patients notified between 1946 and 1955 were retrospectively selected as suitable for thoracoplasty. Of these 72 had the operation, and 187 for one reason or another did not at the time they were thought suitable. The subsequent history of these 187 patients was examined by various criteria, and they seem to be a group generally comparable with those who had the operation. They are dealt with in the periods 1946–51 and 1952–55, as in the later period antibiotic treatment on modern lines was generally available. With the date of suitability for thoracoplasty as a datum line, the period of loss of work, sputum conversion, working capacity and radiographic fate were selected as subjects for comparison. In the first, 18% were off work for less than 4 months, 26% for from 4 to 8 months, and 53% for more than 8 months, the rest were unassessable.

Of the 130 patients who were initially sputum positive, in the early group 12·5% were dead, and 4·5% had a positive sputum against 1·5% dead, and 1·5% sputum positive in the more recent group.

Restoration to normal working capacity was achieved when reviewed in December 1957, in 73% and 86%, respectively, though this is an under-estimate as some patients though fit had refused work or had retired.

Radiographically 60% and 74% had improved; 17% and 20% had no change, and 17% and 2·5% became worse. 19% had relapses; of these 25% died: failure of medical judgment and inadequate medical treatment were the main causes for relapse.

With reservations, the fate of these patients is compared with that of Gough's patients [this *Bulletin*, 1958, v. 33, 30] and other thoracoplasty series. This series had 14% dead, 15% relapses and 3% active disease, compared with 8·5%, 21·3% and 8·5% respectively in the medically treated series. These figures refer to the 1947 to 1949 group.

The authors conclude that medical treatment is able to produce results not inferior to those results achieved by thoracoplasty. *F. H. Young*

DREW, Deirdre M. & O'ROURKE, J. **The Future of Thoracoplasty in Pulmonary Tuberculosis.** *Brit J. Tuberculosis.* 1958, Oct., v. 52, No. 4, 319–24. [13 refs.]

Papers giving the results of thoracoplasty in pulmonary tuberculosis which cover an adequate number of cases are common, but this paper tries to utilize the results on 446 patients operated on between 1951 and 1956 to evaluate the use of the operation and its value in the future.

The authors point out correctly that in most surgeons' practice resection has removed a high proportion of the more favourable cases, and thoracoplasty is likely to become a "salvage" operation.

80·9% of patients are considered to have a satisfactory result, but on the 31 patients who have had long term chemotherapy before operation without sputum conversion this figure drops to 51·6%. In those patients with a positive sputum before operation but who had not had long term chemotherapy the figure was 74%. The operative mortality was 12·9%, and 2·1%, respectively. 8 out of the 31 have died (25·8%). It seems probable that most of these patients were excreting resistant bacilli but it is a pity that their sensitivities are not mentioned. There were in the series 33 patients over 45 years of age; of these 3 died of tuberculosis within 3 months of operation. 75·8% are satisfactory.

It is deduced that owing to the material on which thoracoplasties will be used in the future, an increased mortality and less favourable results will be obtained, but with careful selection the results will still be worth while. *F. H. Young*

RONALD, A. C. & STITT, J. F. **Effect of Adequate Long-Term Chemotherapy on Relapse in Pulmonary Tuberculosis.** *Brit. J. Tuberculosis.* 1958, Oct., v. 52, No. 4, 313–18.

This is a retrospective review of 850 patients who were discharged from sanatorium from January 1954 to June 1956, and who were considered to have had adequate and successful long term chemotherapy—a minimum of 1 year—usually with the 3 standard drugs. 648 were traced in June 1958; 20 had relapsed (5 who were readmitted for pulmonary symptoms but in whom no reactivation of tuberculosis could be found are omitted). This gives 3·1% of relapses. Even with minimal cases the period of sanatorium treatment was usually over 1 year. 127 patients underwent surgery. 7 patients relapsed within 1 year, and a further 9 within 2 years.

Of the 20 who relapsed, 11 were fully sensitive to all drugs, 4 partially resistant, and 5 undetermined, at the start of treatment.

5·5% of patients over 40 years of age, against 2% under 40 years of age, relapsed.

Of the 20 relapse patients 10 have been re-treated satisfactorily. The relapse rate of 3·1% is compared with a relapse rate of 10–20% in minimal cases, and 40% in advanced cases in the immediate pre-antibiotic era, though this is higher than has occurred in patients treated at the Brompton Hospital, London. *F. H. Young*

SZULKIN, Elżbieta & OSTROWSKA, Teresa. Kontrola państwowa (seryjna) liofilizowanej szczepionki BCG. **[State Control in Poland of the Lyophilized BCG Vaccines]** *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 1, 77–84.

The English summary appended to the paper is as follows:—

"Lyophilized BCG vaccine for oral and interdermal use are produced in Poland. Principles and methods applied in the evaluation of the vaccine by the state control are presented. Results of examination of about 2000 lots of both vaccines produced in the time from 1955 are given, 1500 lots, each one containing at least 1.5 millions living particles pro 1 mg were released. Numbers of living particles in the oral vaccine stated immediately after production and two to three weeks later were compared. A decrease of the living particles during this period was more times observed. The differences of this kind were never seen when vaccine for intracutaneous use was examined. The expiration time is limited to 12 months since release. No significant differences in the number of living particles were noticed when Löwenstein medium in test tubes and parallelly in Legroux bottles was used for inoculation and enumeration of living particles."

BÉTHOUX, L. & DUNY, S. Contribution à l'étude de la vaccination anti-tuberculeuse par doses élevées de BCG buccal, chez 200 enfants dont 160 nourrissons nés de parents tuberculeux. **[Oral BCG Vaccination with Large Doses of Vaccine]** *Bull. Acad. Nat. Méd.* 1959, v. 143, Nos. 9/10, 211–16.

Dissatisfied with their experience of vaccinating very young infants by scarification the authors have readopted the original oral method of CALMETTE, only with much larger doses of vaccine than he gave. [Earlier work on this subject by BÉTHOUX was noticed in this *Bulletin*, 1956, v. 31, 268.]

Since 1955 200 contact children, of whom 160 were very young, have been vaccinated by giving 3 doses of freeze-dried BCG vaccine each of 150 mgm. with an interval of 1 month between doses. The vaccine was mixed with sweetened boiled water and given from a feeding bottle on an empty stomach. In order to lessen the risk of vomiting no food was given for 1–2 hours afterwards.

Care was taken to vaccinate only non-reactor children and a double skin-test (heat-killed BCG and tuberculin 10 TU) was done several days before vaccination and any child reacting excluded. The tests were repeated 2 weeks after each dose of vaccine. X-ray and blood examinations were done before vaccination in every case. No child was vaccinated who was not completely healthy.

Both tests became positive in 80% simultaneously or nearly so 45–75 days after the first dose of vaccine; the BCG test usually became positive before the tuberculin test. In 18% the BCG test became positive while the tuberculin test remained negative, and the converse was seen in 3 children. Failure to convert was seen in 1 child.

In the authors' experience the BCG test is more sensitive than the tuberculin test for detecting infection and it is positive in about 98% of those vaccinated by the method described.

The vaccination was well tolerated especially by the 40 children over 3 years of age. Bucco-pharyngeal ulceration and cervical, mediastinal or mesenteric adenitis were not observed. Gastro-enteritis of mild or moderate degree occurred in 20%, especially after the second dose; 2 infants displayed slight anaemia. Bacteriological examination of stools was done and of 313 specimens examined BCG was found in 72.

Lymphocytic meningitis occurred in a child of 6 years 1 month after the second dose of vaccine; no specific cause could be discovered. Another child aged 23 months in contact with his tuberculous father was vaccinated after a single skin test; 6 days after the second dose erythema nodosum developed. [His tuberculin state at this time is not mentioned.] The condition was attributed to pre-vaccinal infection by the father and it was thought that the child had been vaccinated in the pre-allergic phase of this infection.

There was poor success in the follow-up and only 44 of the 200 children attended: 2 at 10 months, 15 at 12–18 months, 11 at 18–24 months and 16 at 24–33 months. All had at least the BCG test and 37 reacted either to it or the Mantoux test. The authors recommend the method as simple, harmless and acceptable to parents. *H. G. Calwell*

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GERVOIS, M. & LEBEURRE, R. Comment éviter les adénites suppurées post-vaccinales après administration parentérale de B.C.G. **[The Avoidance of Gland Abscesses after BCG Vaccination]** *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1959, Jan.–Feb., v. 7, No. 1, 46–50. [10 refs.]

The occurrence of suppuration in a regional lymph gland is a troublesome though not serious complication of BCG vaccination which may bring discredit on a valuable preventive measure. The age of the child vaccinated and the method of vaccination both influence the frequency with which it occurs.

It was reported by R. MANDE, C. FILLASTRE and A. HERRAULT (*Rev. Tuberculose*, Paris, 1958, v. 22, 165) that lymph gland abscess occurred in 1·24% of children under 2 years, in 0·36% between 2 and 5 years, in 0·27% between 5 and 10 years, in 0·1% between 10 and 15 years and 0·03% thereafter. The complication was less frequent (0·3%) in children under 2 when vaccination was done by scarification than when it was done by intradermal injection (1·58%). [PURSER, this *Bulletin*, 1954, v. 29, 473, reported an incidence of 0·72% in newborn.]

The authors have studied the vaccination records of 2 series of vaccinations in France, all done by scarification. The first series comprised 16,550 vaccinations done between 1947 and 1953 and the second 55,205 between 1955 and 1957. The children in the first series were of school age and the incidence of gland abscess was 0·06% (10 cases). Suppuration occurred 3 weeks to 3 months after vaccination in 8 cases and in 1 case 1 year after vaccination on the occasion of a Mantoux test. The vaccinal organism was recovered several times; secondary infection was never seen.

In 1955 the incidence was 0·04% (3 in 6,888) since when the complication has not been seen in the Lille centre where Lebeurre works. Incidences of 0·09, 0·02 and 0·006% for 1955, 1956 and 1957, respectively, were reported from other centres.

The vaccine used was fresh BCG vaccine from the Pasteur Institute, Paris; 6 scarifications, each of 1 cm., were made in children aged 6–10 years and each of 1·5 cm. in those aged 10–15. More recently 8 scarifications, each of 2 cm. in length, were made in persons aged more than 14 years.

It was observed that suppurative adenitis became less frequent the more superficial the scarification. The post-vaccinal conversion rate was unchanged throughout. The latest series of children included 972 under the age of 2 years. These were vaccinated by 3 scarifications each not exceeding 1 cm. Suppurative adenitis did not occur in any infant.

Exact pre-vaccinal tuberculin testing, careful clinical examination and exact measurement of scarifications at a level at which blood is not drawn will almost completely eliminate post-vaccinal gland abscess formation. *H. G. Calwell*

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HINDEN, E. **Fatal Miliary Tuberculosis in an Immunised Child.** *Brit. J. Tuberculosis.* 1958, July, v. 52, No. 3, 264–8.

A male infant aged 3 months was vaccinated with BCG. [No mention is made of his pre-vaccinal tuberculin state.] The vaccination lesion developed normally, and 5 weeks after vaccination he was found to have a positive tuberculin reaction (Mantoux 10 TU, 10 mm.).

The family history showed that an uncle, who had a tuberculous hip had died of Addison's disease during the first year of the child's life. This man's widow suffered from pulmonary tuberculosis and was being neither treated nor supervised as she had refused both. The infant visited the house where she lived but according to his mother he had never been in contact with her.

In March 1955 when aged 1½ years the child was examined at a hospital because of loss of weight and fretfulness. He had a low fever, and X-ray examination showed appearances of bronchopneumonia or early miliary disease of the lungs. Sonne dysentery supervened but after it had passed the child seemed better. The Mantoux test (10 TU) was negative early in May and towards the end of May he was discharged apparently quite recovered.

Early in June he appeared well but the skiagram showed appearances suggestive of tuberculosis; siderosis was a possibility but sarcoidosis was considered unlikely. 3 months later he had lost weight and was coughing; the skiagram showed widespread mottling as before and hilar calcification. He was readmitted to hospital and the Mantoux reaction to 10 TU was negative but positive to 100 TU 2 days later. On September 22 it was considered that the condition was miliary tuberculosis.

Full treatment was carried out with streptomycin and isoniazid and later with Dipasic and Achromycin [tetracycline] but without benefit and he died in November after 8 months' illness.

From September 17 to 23 3 gastric washings were negative for tubercle bacilli; on the 26th the report was "Tb. scanty positive", but the next 3 were again negative. The specimen of the 23rd gave no growth on culture and failed to infect a guineapig. No evidence of sarcoidosis was found and the failure of chemotherapy could not be explained on the grounds of agammaglobinaemia.

Post-mortem examination showed innumerable palpable tubercles in the lungs. There was no lymphadenitis. The heart, liver, spleen and kidneys showed evidence of right heart failure. Emulsions of lung, axillary and pulmonary hilar glands were inoculated into 3 guineapigs none of which developed tuberculosis.

The possibility of the disease having been caused by BCG is discussed and dismissed. The generalized glandular enlargement with massive bacillary colonization which was such a feature of the BCG fatalities reported from Scandinavia was absent, no viable organisms were recovered post-mortem, and the histological appearances were those of obvious tuberculosis. Death was due to heart failure caused by pulmonary scarring and not to failure of chemotherapy.

*H. G. Calwell*

Coltart, Margaret [M.A., A.M.I.A.], Raine, Helen [B.A.] & Harrison, Elizabeth. **Social Work in Tuberculosis.**

This book was reviewed on p. 695.

## VENEREAL DISEASES

Soquel, J. A., Hosking, W. O., Montgomery, C. H. & Laurentz, F. K. **Epidemiologic Study of Infectious Syphilis.** *Southern Med. J.* 1959, Feb., v. 52, No. 2, 199–203, 1 fig.

This story starts with a man found to have syphilis as a result of a routine blood test; epidemiologic investigation involved over 300 persons; within 4 months 36 infected persons were found and after 7 months 63.

The chain of infection is well shown in a chart; in several cases delay resulted in more persons being infected. 2 tables show contact indexes for infectious syphilis and the age distribution of males and females; the former varied from 6·39 to 4·77 and females tended to be younger than males.

All diagnosed cases and *known contacts* were treated with 2·4 mega units of benzathine penicillin; only so can the chain of infection be broken.

A study of the chart and the explanation in the text of how the infection was spread is most revealing. The authors claim that the treatment of contacts of infectious syphilis is justifiable on epidemiologic grounds and that rapid follow-up and treatment is the only method of eradicating the disease. *T. E. Osmond*

Castets, M. La sérologie de la syphilis chez les Africains de Dakar. [**The Serology of Syphilis in Africans in Dakar**] *Bull. Méd. de l'A.O.F.* Dakar. 1958, Oct.–Dec., v. 3, No. 4, 381–98. [30 refs.]

In Europe and America the incidence of syphilis is about 1%; in black races, however, a study of the literature shows that it varies from 15 to 40% or more, judged by the results of serum tests. The author sets out to explain this. Technical errors and certain tropical diseases [all of which are well known] account for a good deal of the difference; however, this author tries to show that congenital syphilis is hardly ever seen in Dakar.

He examined 300 pregnant African women and their babies (blood from the latter was obtained from the umbilical cord or superior longitudinal sinus) by means of the Kline, VDRL, and Kolmer quantitative tests [using presumably cardiolipin antigen in all cases]. Of the 300 mothers 35 were sero-positive and of the 307 babies 32 were sero-positive; a baby was never sero-positive when the mother was sero-negative. The Kline reaction proved the most sensitive followed by the Kolmer and VDRL in that order; only 8 of the sero-positive mothers had received antisyphilitic treatment; in general babies tended to give similar reactions to the mother but the the former were nearly always weaker.

20 of the 32 positive babies were followed up; all became sero-negative in a maximum period of 4 months; if a baby is sero-positive at birth and serum reactions weaken it is certain that it is not syphilitic; the reagin (as also immobilizins) is passively transferred through the placenta.

No explanation is offered of the fact that though sero-positivity is high in Dakar active or congenital syphilis is rarely seen by clinicians.

A large amount of detail is set out in 7 tables.

[The author appears to be satisfied that quantitative serum reactions in which cardiolipin antigen is used are completely specific; is he not over sanguine?]

*T. E. Osmond*

Koschucharoff, P. Ein neues Verfahren zur Ausführung der Original Wa R mit geringen Mengen peripheren Blutes. [**A New Technique for the Original Wassermann Reaction with Small Amounts of Peripheral Blood**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 7/8, 614–18. [18 refs.]

The author carried out the test with 0·2 ml. blood obtained from the finger or ear lobe and received into 0·8 ml. normal saline solution to which an anticoagulant had been added. After removal of the cells the serum dilution was inactivated and the test carried out by the standard technique with one-quarter amounts of reagents.

Not all anticoagulants are suitable. Those more commonly used in laboratory work are anticomplimentary. Heparin in a dilution of 1/10,000 and even stronger was found satisfactory.

Results obtained by this method were compared with results obtained by using serum and reagents in the standard technique, and were found to agree.

*P. A. Clearkin*

SCHNEEWEISS, U. Neuere experimentelle Erkenntnisse auf dem Gebiete der serologischen Syphilisdiagnostik. [**More Recent Experimental Findings in respect of Serological Diagnosis of Syphilis**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1958, Sept.–Oct.–Nov.–Dec., v. 4, Nos. 5/6, 329–41, 4 figs.

In view of the high incidence of syphilis in the period about the termination of the second World War and its treatment with modern antibiotics, the medical profession in Germany is faced with the possibility of a wide latent syphilitic infection involving the vascular and nervous system.

This state of affairs makes the evaluation of the numerous sero-logical tests available for the support of a clinical diagnosis of great importance. The reactions compared have been the Meinicke precipitation, the cardiolipin micro-flocculation, the pallida and cardiolipin complement-fixation reactions and, finally, the Nelson treponema immobilization test which alone of these depends on antibodies specific to man-pathogenic treponemata.

Applying these reactions to large groups of people who were capable of pursuing their normal occupation, appeared as blood donors, or were clinical cases of syphilis, the author reaches the conclusions that the cardiolipin micro-flocculation test was the most sensitive and specific of the tests depending on the presence of "reagin" in the serum but that the Nelson test was the most valuable especially in detecting syphilitic infection in the latent phase.

In a graph in which the rise of the classical lipoid antigen and the specific treponemal antigens are compared, it is shown that whereas the former rises rapidly to a maximum in the secondary stage and then falls away during the later period to rise again to some extent in the tertiary stage, the specific treponemal reaction rises more slowly but continuously to reach a maximum in the latent period between the secondary and tertiary stages.

*J. W. McLeod*

BERLINGHOFF, W. Moderne serologische Syphilisdiagnostik und ihre Bedeutung für den Kliniker. [**The Modern Serological Diagnosis of Syphilis and its Significance for the Clinician**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1958, Sept.–Oct.–Nov.–Dec., v. 4, Nos. 5/6, 341–52, 1 fig. [16 refs.]
Diskussionsbemerkungen zu dem Thema "Lues-Serologie. [**Discussion**] *Ibid.*, 352–4.

The author presents the results of an elaborate and extensive comparison of the Nelson test with the older serological reactions for syphilis which depend on lipoid antigen and with the pallida reaction which depends on an antibody developed against protein spirochaetal antigen which is not specific.

The general outcome of these tests is to show that there are a considerable number of syphilitic infections especially in cases of latent and neurosyphilis which escape detection by the reactions depending on lipoid antigen but which are revealed by the Nelson test. This is even more marked in the case of treated cases of syphilis in the latent phase.

Where treatment has been instituted in the early phases of the disease, *i.e.*, the first or second stages or early in the latent phase, the Nelson test is useful in assessing the value of treatment as it disappears when this is successful. When, however, syphilis has persisted into the later stages without treatment or has only undergone treatment relatively late in the disease, the Nelson test remains positive irrespective of treatment. It cannot, therefore, be used as a criterion of the success of treatment in such cases. The difficulties which may arise in the Nelson test are discussed and attention is specially drawn to the fact that normal sera left for any considerable time—24 hours or more—in contact with a rubber stopper will develop bactericidal power for spirochaetes. This sort of error occurs when specimens are sent through the post unless special precautions in transport have been observed. It is desirable to carry out all such tests within 10–12 hours of withdrawal of the specimen.

Data are also given with regard to the value of the modified Nelson test in which a complement-fixation reaction is carried out with the Nichols spirochaete. Such reactions are not so open to artificial flaws as the immobilization test and gave a higher percentage of positives among the Nelson test positive sera than the other methods investigated. This particular form of reaction, however, is considered to require extended observation before it is finally adopted.

In the comparison of various reactions with the Nelson test, the conclusion is reached that the Kahn reaction gives much the highest number of false positives; the cardiolipin reaction and the second Meinicke precipitation reaction give a considerable number; the Wassermann very few and the pallida reaction least of all. On the other hand, unduly weak positives are most often obtained with the classical Wassermann reaction and after it with the pallida reaction, the second Meinicke flocculation reaction and the cardiolipin reaction and, least of all, with the Kahn reaction.

The general conclusion reached from all this is that the classical Wassermann reaction is insufficiently sensitive, that the Kahn reaction is unduly sensitive, and that the cardiolipin complement-fixation reaction and the second Meinicke precipitation reactions are the most reliable of those which depend on lipoid antigen and reagin.

The Nelson test is recognized as the most specific of all the serological tests for syphilis with 2 weak points—slow development in the early stages of syphilis and persistence in late treated syphilis independent of treatment.

*J. W. McLeod*

HARRIS, A., BOSSAK, H. N. & WALLACE, Alwilda L. **Serological Preselection for the *Treponema pallidum* Immobilization Test.** *Pub. Health Lab.* 1959, Jan., v. 17, No. 1, 14–20.

A *Treponema pallidum* immobilization (TPI) service has been set up by the Venereal Disease Research Laboratory; here, owing to the large number of sera submitted and the delay which may occur in reporting, an investigation was carried out to find suitable preselection tests which could render a TPI test unnecessary. A large number of sera were submitted to the VDRL slide, the Kolmer with Reiter protein antigen (KRP) and the TPI tests.

The sera were placed in 7 categories, (a) presumed normal, (b) diseases other than syphilis, (c) untreated primary and secondary syphilis, (d) early syphilis adequately treated, (e) late syphilis adequately treated, (i) biological false positive, clinically, with a previous negative TPI test and (j) the same but without a previous TPI test. In the first 5 categories there was 83% agreement and in the first 2 94%; in (i) VDRL was positive in 48%, KRP positive in 9% and TPI positive in 4·3%; in (j) the respective figures were 44, 35 and 37. Of all sera TPI positive the VDRL detected 87% and KRP 69%, while the latter 2 combined detected 96%.

Detailed figures of the results of all 3 tests in the various categories of sera are set out in 2 tables.

It is concluded that the preselective use of the VDRL and KRP tests on sera from diagnostic problem patients and those with suggestive evidence of syphilis but untreated would greatly reduce the number of TPI tests necessary. *T. E. Osmond*

TANI, T., MATSUBARA, M., ITO, R. & NAKAMURA, M. **Improvement of the Techniques for *Treponema pallidum* Agglutination Test.** *Japanese J. Med. Sci. & Biol.* 1958, Oct., v. 11, No. 5, 295–305. [30 refs.]

One of the problems involved in this test is the occurrence of non-specific agglutination; to obviate this treatment of the antigen with antiformin [this *Bulletin*, 1952, v. 27, 423] or bleaching powder or heating was tried; treatment of the sera to be tested with hydrochloride acid was also carried out.

Antigens were prepared from syphilitic rabbits' testicles; tissue fragments were removed from testicular suspension by centrifugation and after the suspension had been heated to 65°C. for 2 hours Sorensen's phosphate buffer *p*H 7·4 and Merthiolate to make 1/10,000 were added; the final concentration of spirochaetes was 100–200 million per cc. The treatment of sera by hydrochloric acid consisted of adding 0·8 cc. of N/400 hydrochloric acid to 0·1 cc. of heated serum and centrifuging after 30 minutes.

For the TPA test antigen and sera were mixed and 1 drop of 0·2% saponin added and the whole incubated at 50°C. for 20 hours. The results of tests with chlorine or heat treated antigens are set out in tables in comparison with the Wassermann reaction, the VDRL and Murata tests.

The TPA and WR agreed in 98·8%, the TPA and VDRL in 98·6% and the TPA and Murata in 87·9% of sera from normal persons; in 113 sera from pregnant women TPA and WR agreed in 98·2%; in 145 sera from leprosy patients the WR was positive in 15·9%, the VDRL in 30·6%, the Murata in 12·5% and TPA 15·2%.

In 80 sera from persons diagnosed clinically syphilitic or non-syphilitic TPA agreed in 91·3% and VDRL in 97·5%; in 127 spinal fluids TPA and WR agreed in 98·4%.

It is concluded that the TPA test is equal to other tests for syphilis and helpful in detecting syphilis in leprosy patients.

[The poor standard of English and mistakes in this article make it rather difficult to follow; the results do not suggest that the "improved" TPA test presents any great advantage over standard tests for syphilis.] *T. E. Osmond*

PLAGNOL, H., with the technical collaboration of MALLET. Protidémie et syphilis chez les mères et nouveau-nés Africains à Dakar. [**Blood Proteins and Syphilis in African Mothers and Babies in Dakar**] *Bull. Méd. de l'A.O.F.* Dakar. 1958, Oct.–Dec., v. 3, No. 4, 399–414. [58 refs.]

This article reports the results of biochemical tests of the blood of 152 sero-negative and 19 sero-positive mothers and 149 sero-negative and 18 sero-positive infants as regards total proteins, albumin, various globulins and the albumin/globulin (A/G) ratio. Particular reference is made to pregnancy and to the effect of syphilis; comparisons are made between Africans and Europeans and figures obtained by a number of other investigators are quoted. Thus the article consists of a vast amount of figures which cannot be included in an abstract.

It appears that pregnancy in sero-negative Africans causes a lowering of total protein and albumin, increase of the alpha and beta globulins and slight decrease of gamma globulins with diminished A/G ratio; the newborn baby shows differences from the mother, and in most respects the findings are very like those in white babies. Sero-positive African women show slight increase of total proteins, lowering of albumin and increase of gamma globulins and reversal of A/G ratio (as in Europeans). Sero-positive babies show increase of total proteins and globulins and decrease of albumin. The cord blood (which was used for tests) is essentially the same as the mother's blood but usually contains rather less syphilitic antibodies which tend to disappear within 4 months of birth.

It is assumed that all the sero-positive mothers were syphilitic and the fact that all the babies escaped infection is due to the mothers' infections being old and latent. *T. E. Osmond*

WARD, R. & READ, L. **The Prognosis in Syphilitic Aortic Aneurysm after Treatment with Penicillin.** *Brit. J. Dis. Chest.* 1959, Jan., v. 53, No. 1, 52–6, 4 figs. on pl. [11 refs.]

These authors treated 13 patients (6 males and 7 females) suffering from syphilitic aortic aneurysm with penicillin; 3 died after 20, 26 and 48 months respectively (but not due to rupture of the aneurysm) and the remaining 10 were alive 32 to 74 months after treatment. There were 9 saccular and 4 fusiform aneurysms and the main symptoms were pain, dysphagia and hoarseness. Treatment consisted of 600,000 units of procaine penicillin daily to a total of 20 mega units; potassium iodide did not appear to be of any value; 2 patients had Herxheimer reactions but recovered rapidly; 9 are leading relatively normal lives. The most obvious results of treatment were feeling of well-being, improvement in phonation, disappearance of dysphagia, cessation of haemoptyses and gain in weight. 2 case histories are given in detail with X-ray appearances.

It is suggested that occult lesions elsewhere than in the blood vessels are affected by treatment as well as syphilitic granulation tissue in the aorta [this *Bulletin*, 1951, v. 26, 888].

[The high proportion of females to males is somewhat remarkable; it would be interesting to know how long symptoms had been present in each case before treatment was started.] *T. E. Osmond*

IKEJIANI, O. **Gonococcal Meningitis: a Review of Literature and Report of a Case.** *West African Med. J.* 1958, Sept., v. 7 (n.s.), No. 3, 139–42. [20 refs.]

A review of the literature reveals only 25 reported cases of this disease; possibly other cases occurred before the gonococcus could be identified and were diagnosed as meningococcal meningitis; no doubt the infection spreads from the urethra *via* the blood stream.

The case described was that of a young Nigerian who had had repeated attacks of gonorrhoea and who had failed to react to penicillin and "M & B 760". There was pyrexia (101·8°F.) pulse rate 102, respiration 24; right epididymitis, opisthotonus, and rigidity of the neck; the cerebrospinal fluid contained 28,000 polymorphonuclear leucocytes, protein 1·2 gm.% and sugar 24 mgm.%; the blood contained 24,000 white cells per cmm.

Smears of urethral discharge and spinal fluid showed gonococci; cultures of blood, urethral discharge and spinal fluid [?all] grew organisms which were proved to be gonococci. Intravenous sulphadiazine and penicillin intramuscularly caused no improvement but oxytetracycline 500 mgm. by drip and 500 mgm. orally every 6 hours for 2 days followed by 250 mgm. every 6 hours for a further 6 days brought about rapid improvement. The patient was discharged cured on the 16th day. It seems clear that this strain of gonococcus was resistant to sulphonamides and penicillin.

*T. E. Osmond*

EPSTEIN, E. **Failure of Penicillin in Treatment of Acute Gonorrhea in American Troops in Korea.** *J. Amer. Med. Ass.* 1959, Mar. 7, v. 169, No. 10, 1055–9, 1 fig.

This article recounts the results of treating gonorrhoea with 600,000 units of aqueous procaine penicillin G given intramuscularly daily for 5 days; in 146 patients so treated there were 30 (20%) failures; presumably these were not reinfections since all patients were confined to barracks for 14 days.

Of the 30 failures 17 were treated with oxytetracycline with 2 failures cured by chloramphenicol; the other 13 were re-treated with penicillin with 4 failures cured by oxytetracycline.

Reports of 2 cases are given in detail and the experiences of several other venereologists are quoted.

There seems no doubt that some strains of gonococci are becoming more or less penicillin resistant and therefore careful follow-up of patients is more than ever necessary.

[This article could well have been compressed into less than one-half its volume.] *T. E. Osmond*

MARMELL, M. & PRIGOT, A. **Tetracycline Phosphate Complex in the Treatment of Acute Gonococcal Urethritis in Men.** *Antibiotic Med.* New York. 1959, Feb., v. 6, No. 2, 108–110.

These authors treated 113 male patients suffering from gonorrhoea with tetracycline phosphate in doses varying from 0·75 to 1·50 gm. given in divided doses over 1 day.

The cure rate in 36 patients receiving 1 gm. was over 90% and all of 18 patients receiving 1·50 gm. were cured.

There were no side reactions. *T. E. Osmond*

MARMELL, M. & PRIGOT, A. **Tetracycline with Glucosamine in the Treatment of Gonorrhea in the Male.** *Antibiotic Med.* New York. 1959, Feb., v. 6, No. 2, 117–19.

It was found that it required 1·50 gm. of tetracycline to cure gonorrhoea in the male.

These authors treated 101 patients with tetracycline plus glucosamine and observed 81; the dosage varied from 0·50 to 1·50 gm. given in divided doses over 1 day; 1·0 gm. cured 94% of 42 cases and was thus as effective as 1·50 gm. of tetracycline alone.

*T. E. Osmond*

MARMELL, M. & PRIGOT, A. **The Use of Tetracycline Phosphate Complex in a Venereal Disease Clinic.** *Antibiotics Med.* New York. 1959, Feb., v. 6, No. 2, 111–16, 2 figs.

These authors treated 11 male patients with tetracycline phosphate 1 gm. daily for 6–39 days; the diseases included 7 of lymphogranuloma venereum, 1 of chancroid, 1 of donovanosis, 1 of lymphadenitis and 1 of scrotal abscess (caused by *Staphylococcus aureus*). Details are set out in a table.

Lesions healed in all cases but in the absence of follow-up cure could not be established. There were no side reactions.

It is concluded that this drug is useful in a venereal disease clinic, except for the treatment of syphilis.

*T. E. Osmond*

DEPOORTER, L. Recherches cliniques et expérimentales sur la signification clinique de l'urétrite à *Trichomonas vaginalis* Donné chez la femme. **[Clinical and Experimental Research on the Significance of Urethritis due to** *Trichomonas vaginalis* **in the Female]** *Bruxelles-Méd.* 1959, Apr. 19, v. 39, No. 16, 564–70. [11 refs.]

The presence of this organism (TV) in the urinary tract has been variously estimated as between 25 and 75%. This author found TV in the anterior urethra of 12 out of 14 women with heavily infected vaginas; this was done by means of a "double sound" (to avoid contamination from the vagina); all complained of burning on micturition especially first thing in the morning; in only 7 out of 19 cases were TV found in the posterior urethra. It seems clear that the urethra provides an unsuitable medium for their growth. To demonstrate TV the phase-contrast microscope is the best and "Lash-serum" a suitable medium; the addition of penicillin and streptomycin or tetracycline is useful in suppressing bacterial growth.

When cultures of TV and urine are placed in contact in the incubator at 37°C. the organisms show hydration and movements become more and more sluggish; if these organisms are placed in culture medium they do not seem able to regenerate whereas if they were originally placed in water instead of urine they were able to do so.

In the one the position was irreversible in the other it was reversible. TV were never recovered from the bladder. It seems clear that infection of the urinary tract and also reinfection comes from the vagina and that the reverse does not occur. *T. E. Osmond*

WILLCOX, R. R. **Treatment of Vaginal Thrush with Gyno-Sterosan.** *Brit. J. Clin. Practice.* 1959, Apr., v. 13, No. 4, 259–60. [11 refs.]

21 patients suffering from vaginal thrush were treated with Gyno-Sterosan which is 5 : 7 dichloro-8-hydroxyquinaldine; 2 tablets were inserted in the vagina nightly for 1–4 weeks.

17 patients were followed up and in 11 results were satisfactory; 3 patients developed vaginitis in 2 of which *Trichomonas vaginalis* were found, 1 was not improved after a week when treatment was stopped on account of intolerance and 2 relapsed in spite of retreatment. *T. E. Osmond*

## OTHER COMMUNICABLE DISEASES

*The order of papers in this section is as follows: Tetanus; other diseases.*

LANZO, A. Prednisone nella terapia del tetano. **[Prednisone in the Treatment of Tetanus]** *Arch. Ital. Sci. Med. Trop. e Parassit.* 1959, Feb., v. 40, No. 2, 113–16. English summary (6 lines).

Between 1950 and 1956, the author treated 49 patients suffering from tetanus of whom 24 died, a mortality of 48·8%. Treatment consisted of antitetanic serum, phenobarbitone and chloralhydrate, and penicillin. In 1957 and 1958, he treated 15 patients and only one died, a mortality of 6·6%. Chlorpromazine 25 mgm. every 6 hours was used instead of, or possibly in addition to, phenobarbitone and chloralhydrate, and prednisone 4 mgm. every 6 hours by mouth, or 10 mgm. every 12 hours intramuscularly, was added to the treatment. The author attributes all the improvement to the prednisone. Temperatures fell and the patients felt better more quickly and they seemed more able to stand the convulsions. No details are given whereby one can compare age distribution or severity of cases before or after the introduction of prednisone, but the author states that even apparently hopeless cases recovered and that he had come to regard the disease as having normally a benign course. *A. B. Christie*

ACKLAND, T. H. **Tetanus Prophylaxis.** *Med. J. Australia.* 1959, Feb. 7, v. 1, No. 6, 185–8. [11 refs.]

This is a discussion of the principles on which a tetanus immunization programme should be based. Stress is laid on the facts that active is superior to passive immunity, that a clinical attack does not give rise to immunity, that injected antitoxin disappears rapidly in patients who have had previous injections of antitoxin, and that skin sensitivity is an unreliable index of general sensitivity. The author pleads for a hospital immunization programme along with a universal personal record system. *A. B. Christie*

WIENER, S., PATTERSON, R. W. & MACKENZIE, E. F. **Persistence of Tetanus Antitoxin in Children Two Years after a Third Dose of Tetanus Toxoid.** *Med. J. Australia.* 1959, Feb. 7, v. 1, No. 6, 188–9.

The titre of antitoxin in the blood of 29 children bled 2 years after a third or booster dose of tetanus toxoid was in all the children over 0·1 unit per millilitre. A variety of antigens was used for the third dose, including fluid and adsorbed toxoid, and all were satisfactory. The mean titre 2 years after a third dose was 4 times higher than the mean titre 6 months after the second dose.

[See also this *Bulletin*, 1955, v. 30, 1023.]
*A. B. Christie*

LEBEDEV, A. D. **Routes of Infection of Man with Haemorrhagic Nephroso-Nephritis in the Yaroslavl Oblast.** *Problems of Virology.* London. 1958, v. 3, No. 4, 227–30. [Translated from Russian.]

This is a shortened version of an earlier paper [this *Bulletin*, 1959, v. 34, 630]. It is an epidemiological study of an area in which there were 234 cases in 6 years. Infections of man may be due to contact with excreta of wild rodents while transmission between rodents may be by gamasid mites [but there is no experimental evidence to support either mechanism].
*C. E. Gordon Smith*

## ZOONOSES

*In this section the abstracts are arranged as far as possible in the following order:—General; Anthrax; Brucellosis; Tularaemia; Leptospirosis; Ornithosis; Others.*

*For such tropical diseases as Trypanosomiasis, Leishmaniasis, Rickettsial Fevers, Yellow Fever, Plague, etc., see* TROPICAL DISEASES BULLETIN.

KENDALL, C. E. **Occupational Anthrax in the United States.** *J. Occupational Med.* Chicago. 1959, Mar., v. 1, No. 3, 174–7. [16 refs.]

In this paper there is a general review of anthrax which occurs in nearly all areas of the world in which good animal disease control programmes are lacking. Short descriptions are given here of the disease in animals and in man, the different ways by which the disease can be spread and the methods of control of zoonotic anthrax which are used in the United States. At present 40 to 50 cases of human anthrax are reported annually in the United States most of which are of the cutaneous form of the disease. From 1939–49, 80% of cases were industrial and 14·5% were agricultural. A table sets out a list of 18 types of industrial workers who are potentially exposed to anthrax infection. Of the different sources of infection goat hair was in 1955–6 by far the most common in causing human disease. The occupational factors which increase the chances of infection are mentioned and there is a long description of control measures which it is suggested would reduce the incidence of anthrax in the United States. In this connexion there is reference to the Duckering process of sterilization of hair and wool entering Liverpool, England, which "could be applied with equal success in the United States" where, however, it seems not to be applicable because its high initial cost would raise unduly the price of processed materials. *M. E. Delafield*

KHAIKINA, B. G. **The Detection of Bacterial Antigen in the Blood of a Brucellosis Patient.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 5, 715–20. [Translated from Russian.]

The author claims to be able to detect bacterial antigen produced in sera by means of a special complement-fixation reaction. 384 sera from 185 patients suffering from brucellosis were tested. Brucellosis-antigen was found in the blood of 148 patients (79·4%). The number of patients with antigen consistently present was greatest in the case of acute brucellosis, lower in a group of chronic brucellosis and least in subacute brucellosis. After vaccination with a vaccine of live *Brucella* 31 out of 50 showed brucellosis antigen between 10 and 25 days after vaccination, thereafter the percentage fell rapidly to nil after 4 to 7 months whereas the percentage showing antibodies increased from 42·4% in the first month to 60·9% after 10 to 12 months. These results are interpreted as indicating the active multiplication of *Brucella* during a period of 2–3 weeks after vaccination followed by their destruction. Repeated examination of blood in individual patients suffering from brucellosis indicated that in the absence of positive blood cultures an exacerbation of the disease or the development of an abscess containing *Brucella* might be expected if the concentration of antigen in the blood rose. Absence of antigen in the presence of positive blood cultures indicated a poor reaction on the part of the host. The presence of both live *Brucella* and antigen are characteristic of an acute illness with an adequate defence mechanism causing the death of large numbers of *Brucella*. When immunity increases the rising antibody curve intersects the falling antigen curve, parallel curves characterize the chronic stage. *Frederick J. Wright*

TREVER, R. W., CLUFF, L. E.; PEELER, R. N.; BENNETT, I. L., Jr.; IMBODEN, J. B.; CANTER, A. **Brucellosis. I. Laboratory-Acquired Acute Infection** [TREVER, CLUFF, PEELER & BENNETT]. *Arch. Intern. Med.* 1959, Mar., v. 103, No. 3, 381–97, 10 figs. [24 refs.] **II. Medical Aspects of Delayed Convalescence** [CLUFF, TREVER, IMBODEN & CANTER]. *Ibid.*, 398–405. **III. Psychologic Aspects of Delayed Convalescence** [IMBODEN, CANTER, CLUFF & TREVER]. *Ibid.*, 406–14.

I. It is notoriously easy to acquire brucellosis accidentally in a bacteriological laboratory. The authors have taken advantage of these mishaps to make valuable observations on 60 patients in whom *Brucella suis* or *Br. melitensis* infection was acquired in the laboratory after routine clinical and serological examinations had been carried out at 6-month intervals *before* the infection was acquired and who were uniformly observed and investigated subsequently. *Br. suis* was isolated in 30 and *Br. melitensis* in 14. In 2 the species of the organism was not defined. In the remainder the diagnosis was established by a rise of serum agglutinins to a titre of 1 : 100 or greater. [17 of the cases were previously reported by HOWE *et al.*, this *Bulletin*, 1947, v. 22, 568.] The incubation period was usually between 4 to 8 weeks. Physical signs were few in the acute stage, fever in 54 being the most frequent, splenomegaly being found in only 6 (3 tender) and hepatomegaly in 8 (4 tender). The agglutinin titre *uniformly* rose very early in the course of the infection and was almost invariably positive by the time of the onset of symptoms. Skin testing appeared to cause little change in the agglutinin titres except in 4 cases. 13 patients with negative skin tests before becoming ill all showed positive skin tests when tested at intervals from the day of onset to 14 months after recovery. In 7 patients who had been skin tested months before the illness an area of erythema and induration appeared at the site of the test during the illness and in 1 the reaction led to an indolent ulcer which took 3 months to heal. The pattern of serological response varied. Of 39 followed for over a year 15 showed a rise in agglutinins to a high level gradually falling to below 1 : 100 during the next few months, in 11 a sustained elevation above 1 : 100 was observed, and in 13 one or more secondary rises occurred usually in association with a recurrence of fever and bacteriaemia. The different forms of chemotherapy used did not produce statistically different results.

Chronic brucellosis for the purpose of these studies was defined as the persistence of such symptoms as malaise, fatigue, myalgia, arthralgia, backache and feverishness for a period of 1 year or more after the acute illness, unassociated with demonstrable bacteriaemia, changing serological titre or physical abnormalities. No less than 24 of the 60 patients observed fell into this group. There were no consistent differences in the acute illness or in its serological response in these 24 compared with the 36 who recovered full health within a year.

II. The second paper analyses 16 of these 24 who were available for review. At the time of the study 6 had recovered and are referred to as the *chronic-recovered* group, the other 10 as the *chronic-symptomatic* group. In addition 8 of the *acute-recovered* group (from the original 60) were studied for comparison. No clinical or serological differences in the groups could be discovered and electro-encephalography failed to show any evidence of organic brain damage in chronic brucellosis.

III. The third paper deals with the psychological aspects of the illness in the 24 subjects of the previous study. The analysis of the data revealed emotional disturbance, especially depression, in the chronically ill and that the emotional disturbance was more related to the pre-illness personality structure than to the stress of the illness.

[These useful studies on " chronic brucellosis " indicate that the name as defined by the authors is probably a misnomer for psychological illness precipitated by brucellosis. The danger of an incorrect diagnosis of a psychological illness being made when the symptoms are due to active and demonstrable brucellosis still remains. The early appearance of agglutinins in acute brucellosis and the variable response, if any, of their titre to skin testing are other valuable findings. The observations are limited to *Br. melitensis* and *Br. suis* infections.] *Frederick J. Wright*

ZAMMIT, F. **Undulant Fever Spondylitis.** *Brit. J. Radiol.* 1958, Dec., v. 31, No. 372, 683–90, 10 figs. [17 refs.]

During 1947–54 6,301 cases of brucellosis were reported in Malta where the disease is caused by *Brucella melitensis* acquired from goats. In the same period 115 patients were diagnosed in the orthopaedic department of St. Luke's Hospital, Malta, as suffering from brucellar spondylitis and of these 62 showed radiological signs of disease in the spine although the intervertebral facets were rarely affected. Pain in the back may be very severe before abnormal signs are seen in radiographs. The author analyses the findings in the 62 patients in whom radiographic changes were seen. A constant and the earliest symptom is pain localized to the affected region and in 60% there was also pain referred to the limbs or as a girdle pain. Localized tenderness occurred in 20%. In 8 patients there were signs of cord compression in association with bone changes and in another case a peridural abscess caused a block on myelography in the absence of bone changes. The regional distribution of lesions was cervical 5, dorsal 16, combined dorsal and lumbar 4, lumbar 37. The 4th lumbar vertebra was the most commonly affected. The characteristic lesions of the vertebrae are described in detail and illustrated. Narrowing of the disk space was found to be the general rule and an early sign but permanent total disappearance of the disk space with bony ankylosis was not observed. Proliferative marginal reactions are characteristic and may lead to the formation of a complete curved bridge between 2 vertebrae. Changes in the intervertebral joints were rarely demonstrable radiographically. The differential diagnosis from tuberculosis, staphylococcal osteomyelitis, actinomycosis, Scheuermann's disease and osteoarthritis is discussed. [A valuable contribution based on abundant clinical and radiographic material.] *Frederick J. Wright*

WIDDICOMBE, J. G., HUGHES, R. & MAY, A. J. **Physical Changes in the Lungs during Respiratory Infection with** *Brucella suis*. *Brit. J. Exper. Path.* 1959, Apr., v. 40, No. 2, 125–32, 4 figs. [19 refs.]

Studies on the mechanics of the lung in disease have been largely limited to chronic disorders and to pneumonia. In pneumonia the lungs are abnormally stiff not only because of consolidation but also probably because the ventilated parts show increased resistance to distension. The experiments reported here apply strictly only to *Brucella suis* infection of rabbits but the findings may bear a general relation to other acute and subacute infections in man. The rabbits were infected with controlled doses of *Br. suis* inhaled into the lungs as single organisms. In spite of some thickening and cellular infiltration of the alveoli, there was no evidence of increased rigidity of the lungs in the eupnoeic range of inflation volumes and there was a decrease in rigidity above that range. There was a considerable increase in pulmonary capillary permeability. It is postulated that if other organisms also cause increased distensibility of lungs these changes may lead to emphysema. *Frederick J. Wright*

VAN METRE, T. E., Jr. & KADULL, P. J. **Laboratory-Acquired Tularemia in Vaccinated Individuals: a Report of 62 Cases.** *Ann. Intern. Med.* 1959, Mar., v. 50, No. 3, 621–32, 2 figs. [17 refs.]

There is a high incidence of tularaemia among non-vaccinated laboratory workers exposed to *Brucella tularensis*. There have been previous reports of ulceroglandular tularaemia in laboratory workers presumably immunized by prior infection and also reports of tularaemia in vaccinated personnel. Of the 62 cases reported by the present authors, 9 exhibited ulceroglandular disease, 43 were of the typhoidal type and 10 were asymptomatic. The ulceroglandular lesions began as erythematous papules at the sites of introduction of *Br. tularensis* through accidental injuries of the skin or mucous membrane. The papules progressed to ulceration and the regional lymph glands became enlarged and tender. In 6 patients the organism was recovered from the local lesion. The typhoidal type was more common and was sometimes associated with clinical or radiological evidence of pulmonary or upper respiratory involvement. The diagnosis was confirmed by the culture of the organism or an agglutination titre of 1 : 1,280 or more observed 2 months or more after the last immunization. Recovery was spontaneous in patients with mild infections. Treatment of the remainder was not entirely satisfactory. In general the use of streptomycin was satisfactory but there was some evidence that chronic disabilities, which only followed the typhoidal type of illness, were more frequent if chemotherapy was not given during the first month. No chronic illness occurred in patients given 3-day or more treatment with a combination of streptomycin and chlortetracycline during the first month. There was some evidence that prior vaccination modified the course of tularaemia. *Frederick J. Wright*

STOLZE, E., SCHAAD, J. D. G. & BOOL, P. H. **Weil's Disease associated with Pancreatic Necrosis. Report on a Case.** *Trop. & Geograph. Med.* Amsterdam. 1959, Mar., v. 11, No. 1, 93–5. [11 refs.]

MELZER, H. Zur Epidemiologie und Klinik der Ornithose. **[Epidemiological and Clinical Aspects of Ornithosis]** *Deut. med. Woch.* 1959, Apr. 3, v. 84, No. 14, 664–73, 675, 707, 3 charts & 3 figs. on pl. [61 refs.]

This is a reasonably up-to-date general article on the subject. 28 proved and 9 probable cases in the Wuppertal area are discussed, mostly in detail, with laboratory findings. *S. P. Bedson*

BAYLET, R. J., GILBERT-DESVALLONS, Y. & LE TREUT, A. Nouveau cas de néo-rickettsiose en A.O.F. **[New Case of New-Rickettsial Disease in French West Africa]** *Bull. Soc. Path. Exot.* 1958, May–June, v. 51, No. 3, 301–4.

This is the description of an acute exanthematous fever, of short duration and with enlargement of the spleen, in a French naval airman shortly after his arrival in Dakar. Serological evidence attributed the condition to a member of the "neo-rickettsiae" of Giroud. The source of infection was not discovered. *S. P. Bedson*

# Diseases due to Fungi

*For papers on systematic mycology, see the section in Bacteriology, below. Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the* TROPICAL DISEASES BULLETIN

KASHKIN, P. N. **Review of Works on Medical Mycology published in the USSR between 1946–1956.** *Mycopathologia.* The Hague. 1959, Mar. 31, v. 10, No. 3, 227–68. [Numerous refs.]

RIETH, H. **A Diagnostic Diagram of Mycoses and Mycetes.** *Mycopathologia.* The Hague. 1959, Mar. 31, v. 10, No. 3, 223–6.

This is a large explanatory diagram in colour, which must be seen in the original.

See also p. 774, BUGYI **[Coniomycosis of Rice Workers]**.

CONN, Nancy K., CREAN, G. P., MACCABE, A. F. & MACLEAN, N. **Systemic Candidiasis and Endocarditis due to** *C. tropicalis. Brit. Med. J.* 1959, Apr. 11, 944–7, 1 chart & 6 figs. on pl. [29 refs.]

After a partial gastrectomy for a simple ulcer and, one month later, a further operation for obstruction at the stoma, a woman of 61 years suffered persistent pyuria and fever. *Escherichia coli, Proteus vulgaris* and *Pseudomonas pyocyanea* were cultured on 5 different occasions from catheter specimens of her urine and she received 28 gm. streptomycin, 28 mega units of penicillin and 8 gm. oxytetracycline over a period of 57 days. Because of her poor condition, intravenous infusions of 20% glucose saline had to be administered over a prolonged period and 37·5 mgm. cortisone was given daily during the last 14 days, for a resistant arthralgia. In spite of treatment, high fever and rigors persisted; she developed uraemia and died. During the last week of her life blood cultures yielded a growth of *Candida tropicalis* on 3 occasions.

At necropsy numerous yellow abscesses were present in both kidneys and there was a fibrino-purulent exudate between the anterior wall of the stomach and the underside of the liver. The heart was dilated and large, flat, yellow-grey vegetations were found on the right atrial endocardium. There were smaller vegetations on the left ventricular endocardium and on the trunk of the pulmonary artery. Direct smears from all these sites showed candida-like organisms and culture showed them to be *C. tropicalis*.

This appears to be the first published case of endocarditis due to *C. tropicalis* though the authors discuss

14 cases due to other species of candida. 6 of these were in drug addicts. The various clinical factors predisposing to systemic candidiasis are discussed in relationship to the case, particularly the influence of antibiotic therapy, cortisone, the prolonged intravenous administration of glucose saline, and operation on the alimentary tract. *Peter Abbott*

Nityananda, K. **Monilial Granuloma.** *Brit. Med. J.* 1959, Mar. 14, 690–91, 3 figs.

A malnourished 5-year-old girl presented with a crusted granulomatous lesion covering the anterior two-thirds of the scalp. At the same time, the commissures of her mouth were fissured and the mucous membrane was covered with a thick greyish-white exudate. Lesions without crusts were also present on the body. Potassium hydroxide preparations of scrapings from the scalp revealed fine, straight, poorly refractile hyphae together with larger circular bodies, considered to be chlamydospores. The organism was cultured on Sabouraud's dextrose agar and a saline suspension, injected into the ear vein of a rabbit, gave rise to multiple abscesses of the kidney from which *Candida albicans* was recovered.

Monilial granuloma caused by *C. albicans* is a rare specific entity and the author mentions only 15 cases described previously, all in children. In biopsies of the granuloma, marked proliferation of the organism was found in the infected site in contrast with the more common types of moniliasis in which it may be difficult to demonstrate the organism in direct preparations.

The author notes that the case reported by Hauser and Rothman [this *Bulletin*, 1950, v. 25, 704] was strikingly similar to the present one. *Peter Abbott*

Childs, A. J. **Further Clinical Trials of Amphotericin with a Report on the Treatment of a Probable Case of Generalised Moniliasis.** *Scottish Med. J.* Glasgow. 1959, Feb., v. 4, No. 2, 80–83, 1 fig.

"A series of pneumonia patients were treated concurrently with tetracycline and amphotericin. When the dose of amphotericin was 1600 mg. per day, the incidence of *Candida albicans* in throat and sputum did not rise above the admission-day incidence. In a comparable group treated with tetracycline alone, there was a considerable increase of candida in these specimens.

"A probable case of generalised moniliasis successfully treated with amphotericin is reported. The case arose in a diabetic subject who was treated with penicillin and aureomycin for an upper respiratory infection. The rapidity of onset of the infection, and the small total amount of the antibiotic which induced it are noted.

"These findings indicate the suitability of amphotericin as an antifungal antibiotic for both the prevention and treatment of monilial infections."

Ohlwiler, D. A. & Bricker, E. M. *Candida albicans* **Peritonitis successfully treated with Amphotericin B.** *New England J. of Med.* 1959, Mar. 5, v. 260, No. 10, 488–9.

A 69-year-old farmer developed a generalized peritonitis after an extensive operation on the bowel, followed by intensive therapy with penicillin, streptomycin and tetracycline. On the seventh post-operative day, 800 ml. of sero-sanguineous free intraperitoneal fluid was removed and many cream coloured plaques 1 to 5 mm. in diameter were found on the serosa of the bowel. Budding yeast cells were seen in direct smears from the plaques and the peritoneal fluid produced a heavy growth of *Candida albicans.* 130 mgm. of amphotericin B was introduced every 8 hours into a jejunostomy tube for 11 days, after which the patient made a good recovery. No fungus was grown from 6 abdominal wound cultures taken at intervals during the next month. *Peter Abbott*

Noguchi, Y. & Kato, Y. **Effect of Sodium Ethylmercurithiosalicylate on Succinic Dehydrogenase of** *Candida albicans* **and its Clinical Use in Dermatomycoses.** *Yokohama Med. Bull.* 1958, Aug., v. 9, No. 4, 204–8, 1 fig.

The English summary appended to the paper is as follows:—

"Sodium ethylmercurithiosalicylate had powerful antimycotic effects, both fungistatic and fungicidal, comparing with other antimycotic agents.

"Inhibitory effect of the drug on succinic dehydrogenase of *C. albicans* has been shown in the same dilution of the drug as its fungicidal effect has been done.

"Further, the treatment of some dermatomycoses with the drug in absorption ointment revealed excellent result, therefore, we have an opinion that we can evaluate antimycotic effect of mercuric compounds previously by the test of inhibitory effect on succinic dehydrogenase of *C. albicans* without waste of time."

Blankenberg, H. W. & Verhoeff, D. **Mucormycosis of the Lung. A Case without Significant Predisposing Factor.** *Amer. Rev Tuberculosis.* 1959, Mar., v. 79, No. 3, 357–61, 4 figs.

A 23-year-old Negro woman developed what appeared to be lung abscesses in the lower lobes of the right lung. Notwithstanding antibiotic therapy, her condition deteriorated and surgical removal of the middle and lower lobes was performed. The specimen revealed widespread infarction and necrosis of the lung and the presence of hyphae characteristic of mucormycosis invading the tissues and infiltrating the blood vessels. The patient was anaemic but was not, as is usual in mucormycosis, severely debilitated by concomitant disease when the lung infection occurred. Surgical removal of the major lung focus followed by treatment with nystatin led to complete recovery. *Peter Abbott*

Smith, Marthe E., Burnham, D. K. & Black, M. B. **Cerebral Mucormycosis. Report of a Case.** *Arch Pathology.* 1958, Oct., v. 66, No. 4, 468–73, 7 figs. [15 refs.]

See also p. 794, González Benavides, [**Sporotrichosis as Occupational Disease in Potteries**]

DAS-GUPTA, S. N.; SHOME, S. K. **Studies in Medical Mycology. I. On the Occurrence of Mycotic Diseases in Lucknow** [DAS-GUPTA & SHOME]. *Mycopathologia.* The Hague. 1959, Mar. 31, v. 10, No. 3, 177–86. [28 refs.] **II. Candidiasis of Scalp** [SHOME.] *Ibid.*, 187–90, 3 figs.

I. 405 cases of mycotic disease seen at the Skin Department of King George Medical College, Lucknow, are reviewed. 316 were dermatomycoses, 38 *Tinia versicolor*, 30 candidiasis and 21 erythrasma. 97% of the dermatomycoses were due to 4 species of trichophyton; *Trichophyton rubrum*, *T. mentagrophytes*, *T. tonsurans* and *T. verrucosum*. *Candida albicans* was the only *Candida* species isolated.

II. Candidiasis of the scalp due to *Candida albicans* infection is reported for the first time from India.

*Peter Abbott*

PARDO-CASTELLO, V. & TRESPALACIOS, F. **Superficial and Deep Mycoses in Cuba: a Report based on 1,174 Cases.** *Southern Med. J.* 1959, Jan., v. 52, No. 1, 7–15, 6 figs. [40 refs.]

This report reviews 1,174 cases of superficial and deep mycoses seen at the Clinic for Dermatology at the University Hospital in Havana. In most cases the causative organisms were isolated and specific diagnosis correlated with the clinical manifestations in so large a series makes a useful contribution to the subject.

Tinea of the scalp was caused by *Microsporum canis* in 182 out of 249 cases. The treatment of kerion with penicillin locally and systemically was considered most successful. Of 144 cases of onychomycosis 137 were due to *Tinea rubrum* and treatment with 40% salicylic acid plaster, mechanical removal of the nail plate and fungicides, was considered effective though treatment was prolonged for several months.

Dermatophytosis of the feet in 206 patients was due to *Tinea rubrum* (73), *Tinea mentagrophytes* var. *interdigitalis* (65) and *Epidermophyton floccosum* (60). *Candida albicans* accounted for 8 cases.

71 patients with chromoblastomycosis were seen; 70 caused by *Fonsecaea* (*Hormodendrum*) *pedrosoi* and 1 by *Cephalosporium carrionii*. Treatment of early lesions was by surgical excision but in more advanced cases vitamin $D_2$ with potassium iodide gave excellent results.

Also included in the series were 10 patients with sporotrichosis caused by *Sporotrichum schenkii*, 7 with actinomycosis of which 2 gave culture of *Actinomyces bovis*, and 6 with mycetoma of the foot. From the latter *Nocardia brasiliensis* was recovered 3 times, *Nocardia pelletieri* twice and *Monosporium apiospermum* once.

*Peter Abbott*

POLEMANN, G. Durch Mikrosporon gypseum verursachte Mikrosporien. Beitrag zur Biologie des Erregers. [**Dermatophytosis caused by** *Microsporum gypseum*] *Deut. med Woch.* 1959, Apr. 10, v. 84, No. 15, 748, 756–9, 776, 6 figs. (4 on pl.) [35 refs.]

The English summary appended to the paper is as follows:—

"Three cases of infection with Microsporum gypseum on smooth skin are reported. One of them occurred near one eyebrow after an abrasion caused by a fall in the street. The eyebrow is an exceedingly rare site of infection, as only 8 other instances have been reported. The other two cases were of laboratory technicians working with this organism during a study of its metabolism.—*In vitro* studies showed that soil was able to increase the oxygen consumption of Microsporum gypseum due to the stimulating effect of the nitrogen contained within the sand.—Despite the marked contagiousness of Microsporum gypseum and its almost ubiquitous presence in soil, infection is very rare in children and in agricultural and forestry workers. The main spread of the infection is, in fact, via an animal host (e.g. dogs) as the transmitter; soil serves as the reservoir."

EKMEN, H. Türkiyede Histoplasmin hassasiyeti üzerinde bir çalisma. [**A Survey for Histoplasmin Sensitivity in Turkey**] *Türk Ijiyen ve Tecrübî Biyoloji Dergisi.* Ankara. 1958, v. 18, Nos. 2/3, 158–67, 1 map. [20 refs.] English summary.

The general rate was low (5·3–5·6%) except in one village (39·5%).

QUENUM-AHINA, Cyprien. L'histoplasmose africaine à grandes formes. [**Histoplasmosis due to the African Large Form of the Parasite**] 95 pp., illustrated. 1958. Paris: Amédée Legrand & Cie., 93, Boulevard Saint-Germain.

This thesis consists of a review of the published records of cases proved or suspected of being the African large parasite form of histoplasmosis.

The author summarizes the findings in 20 cases (9 confirmed by culture) reported during the years 1919 to 1957. He then gives in detail the clinical and histological findings and the results of culture and experimental animal infection of the 7 cases (4 confirmed by culture) published by CAMAIN *et al.* [this *Bulletin*, 1958, v. 33, (846); *Bull. Soc. Path. Exot.*, 1958, Jan.–Feb., v. 51, No. 1, 83–107]. To these he adds one additional suspected case not confirmed by culture.

In considering the possible epidemiology of the African disease the author reviews the results of histoplasmin sensitivity tests which have been carried out in various parts of Africa and discusses the role played by soil and animals in *Histoplasma capsulatum* infections, particularly in those of the United States.

The validity of the species *H. duboisii* [this *Bulletin*, 1958, v. 33, 235] is examined and the author considers that this fungus should be regarded rather as a variety of *H. capsulatum* than as a new species [see also DUNCAN, this *Bulletin*, 1959, v. 34, 581].

The thesis is concluded by a list of some of the methods that have been employed in the treatment of histoplasmosis.

*Jacqueline Walker*

ARONSON, D. L. & EDWARDS, Phyllis Q. **An Urban Focus of Histoplasmin Sensitivity.** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 83–6, 3 figs. [10 refs.]

Among schoolchildren living in the town of Dalton, N.W. Georgia, the incidence of histoplasmin sensitivity is higher than in those living in the surrounding countryside and surprising variations in the sensitivity of schoolchildren is found within the town itself. The implications of this finding are discussed and it is suggested that histoplasmin sensitivity in human populations may come from infective sources other than those in the soil. *Peter Abbott*

HEINER, D. C. **Diagnosis of Histoplasmosis using Precipitin Reactions in Agar Gel.** *Pediatrics.* Springfield, Ill. 1958, Oct., v. 22, No. 4, Pt. 1, 616–27, 8 figs. [24 refs.]

A relatively simple precipitin agar-gel technique in which histoplasmin antigen is used is described and the results of testing by this means the sera of a number of patients with histoplasmosis or with suspected histoplasmosis are recorded. If no precipitin band is obtained in a preliminary test with crude histoplasmin antigen the serum is reported as being negative; if a precipitin band is obtained, the antibodies responsible for it may be identified in either of two ways: (1) serum of known antibody composition may be placed in a well adjacent to that which contains the test serum or to several wells containing different test serums and the antibodies of these serums identified by fusion of the new precipitin bands with known bands; (2) purified antigen preparations may be used. It is pointed out in favour of this technique, that whereas by using it no false reactions are observed, this cannot be said of complement-fixation tests which are sometimes not accurate in so far as they may give a false-negative reaction in patients with proven histoplasmosis or, conversely, a false-positive reaction in the case of normal sensitized subjects. It would seem, therefore, that, according to the author, the precipitin reaction in agar-gel is more reliable than complement-fixation tests in the diagnosis of histoplasmosis. *C. J. La Touche*

YAMATO, H., HITOMI, H., MAEKAWA, S., MIMURA, K., HAMAZAKI, Y., OGAWA, K. & UEJIMA, A. **A Case of Histoplasmosis. Report 1. Clinical, Mycological and Pathological Observations.** *Acta Med. Okayama.* 1957, Dec., v. 11, No. 4, 347–64, 20 figs. (19 on 4 pls.) [30 refs.]

BJÖRKMAN, S., FRISK, Å., NORDENSTAM, H. & NORHAGEN, Å. **Generalized Histoplasmosis. Clinical and Patho-Anatomic Report of a Fatal Case.** *Acta Med. Scandinavica.* 1959, Feb. 7, v. 163, No. 1, 45–53, 14 figs. (8 coloured) on 5 pls.

This is a detailed clinical and pathological report of a fatal case of generalized histoplasmosis associated with tuberculous infection; the first, as far as the authors know, to have been reported in Scandinavia. The diagnosis was established at autopsy. *Peter Abbott*

HURWITZ, J. K. & PASTOR, B. H. **Pericardial Calcification associated with Histoplasmosis.** *New England J. of Med.* 1959, Mar. 12, v. 260, No. 11, 543–4, 2 figs. [11 refs.]

" Histoplasmosis has been reported to involve many tissues, but in only 4 cases has it been thought to involve the pericardium. A fifth case in which the diagnosis of histoplasmosis was suggested by the finding of negative tuberculin coccidioidin and brucellin skin tests and a markedly positive histoplasmin skin test in a patient with pericardial calcification and pulmonary calcifications is reported. Three of the 4 patients previously described had pericardial calcification.

" It is suggested that routine use of all available skin tests in patients with pericardial disease will lead to increased recognition of the etiologic role of histoplasmosis. When histoplasmin pericarditis is suspected an attempt to culture and identify the fungus should be made."

UTZ, J. P., GERMAN, J. L., LOURIA, D. B., EMMONS, C. W. & BARTTER, F. C. **Pulmonary Aspergillosis with Cavitation. Iodide Therapy associated with an Unusual Electrolyte Disturbance.** *New England J. of Med.* 1959, Feb. 5, v. 260, No. 6, 264–8, 4 figs. [26 refs.]

" *Aspergillus niger* infection is reported in 2 patients with marked cavitation and abscess formation in previously damaged lung tissue.

" Administration of potassium ioidide in dosage of 30 gm. for two and a half weeks to 1 patient and 24 gm. for three and a half weeks to the other (with surgical drainage) was associated with clearing of aspergillus from the sputum and lung tissue or abscess drainage material.

" Treatment with iodides was associated with disturbance in mental status in 1 patient, and with abnormalities in serum electrolytes in both. In both patients hypokalemia, with elevation of serum carbon dioxide content, and hyponatremia developed. One showed hypocalcemia and hypophosphatemia as well."

LITTMAN, M. L. & SCHNEIERSON, S. S. ***Cryptococcus neoformans* in Pigeon Excreta in New York City.** *Amer. J. Hyg.* 1959, Jan., v. 69, No. 1, 49–59, 3 figs. [18 refs.]

" Specimens of pigeon excreta were collected from various indoor and outdoor locations in the 5 boroughs of the City of New York. These were examined for pathogenic fungi by direct plating on liver–spleen glucose blood agar and by incubating at 37 C. *Cryptococcus neoformans*, confirmed by morphological, cultural, biochemical and by virulence studies, was isolated from 72 of 201 specimens examined. *Candida albicans* was found in 12 specimens and *Nocardia asteroides* in one. Neither *Histoplasma capsulatum*, nor *Coccidioides immitis* nor *Blastomyces dermatitidis* was recovered. Positive isolates of *C. neoformans* proved to be widely distributed throughout the boroughs of the City. Excreta collected from indoor pigeon coops were more heavily and more frequently infected with *C. neoformans* than were those obtained from coops in outdoor sites. Twenty-four specimens (65 per cent.) of 37 collected from different pigeon coops in pet shops were positive for *C. neoformans*.

" The 72 ' pigeon ' strains and 20 strains derived from cases of cryptococcal meningitis were identical in their ability to grow at 37 C; to hydrolyze urea at 20 C; to form capsules on *Cryptococcus* capsule agar at 37 C; in their ability to assimilate dextrose, mannose, trehalose, xylose, galactose, maltose, sucrose, inositol, dextrin and starch as sole separate sources of carbon; in failing to assimilate lactose; and in failing to assimilate $KNO_3$ as sole source of nitrogen. Positive identification based upon these characteristics was accomplished within 1 week. All 72 'pigeon' strains and 20 'human' isolates were virulent for white Swiss mice, producing death within 3 to 73 days after the intracerebral injection of single doses of 3,000,000 yeast cells.

"The connection between pigeon excreta and human cryptococcosis is discussed, and measures to reduce the likelihood of exposure to infection with *C. neoformans* are recommended."

ANDERSON, K. & BEECH, Margaret. **Serological Tests for the Early Diagnosis of Cryptococcal Infection.** *Med. J. Australia.* 1958, Nov. 1, v. 2, No. 18, 601–2.

The authors describe a complement-fixation test which may be of value in the early diagnosis of cryptococcal infection in cases where no organisms can be detected microscopically or by culture. Their method is based on that of NEILL, SUGG and MCCAULEY [this *Bulletin*, 1952, v. 27, 161], who demonstrated serologically active material in various body fluids in such a case. Young rabbits were immunized with a cryptococcal vaccine made with a strain of *Cryptococcus neoformans* recovered from a fatal case of cryptococcal meningitis. Details of 2 complement-fixation methods, a Wasserman tube technique and a Perspex plate technique, are given, with sera recovered from these immunized rabbits. 2 fluids from confirmed cases of cryptococcal meningitis when tested by the Wasserman tube method gave, in the one case, a titre of 1:160 and in the other a titre greater than 1:160. 23 fluids from patients without disease of the central nervous system produced negative results. *C. J. La Touche*

AINSWORTH, G. C. [Ph.D., F.L.S.] & AUSTWICK, P. K. C. [B.Sc., F.L.S.] **Fungal Diseases of Animals.**

This book was reviewed on p. 694.

SEGRETAIN, G. *et al.*, Diagnostic de Laboratoire en mycologie médicale. **[Laboratory Diagnosis in Medical Mycology]**

This book was reviewed on p. 595.

# Rheumatic Diseases

OGBURN, C. A., HARRIS, T. N. & HARRIS, Susanna. **The Determination of Streptococcal Antiproteinase Titers in Sera of Patients with Rheumatic Fever and Streptococcal Infection.** *J. Immunology.* 1958, Nov., v. 81, No. 5, 396–403, 3 figs. [10 refs.]

Antibody titres to the streptococcal proteinase were determined by testing the sera for (1) power to inhibit the activity of proteinase in clotting milk, (2) complement-fixing with proteinase as the antigen, and (3) agglutination of tannic acid treated red cells sensitized with proteinase. All 3 methods gave generally consistent results, but the haemagglutination method appeared the most sensitive, and was used in further studies. Of 101 normal children 39% had titres less than 12 and the maximum observed was 384. Patients convalescent from various virus infections tended to have higher titres. During an attack of scarlet fever, 51 of 100 children showed no rise in titre and few showed more than a 4-fold rise. In acute rheumatic fever the geometric mean titre was 420 compared with 66 for quiescent rheumatic fever. It is suggested that this difference is greater than for some other streptococcal antibodies [but comparative data for the others are not presented]. *R. E. O. Williams*

MORTIMER, E. A., Jr., VAISMAN, S., VIGNAU, A., GUASCH, J., SCHUSTER, A., RAKITA, L., KRAUSE, R. M., ROBERTS, R. & RAMMELKAMP, C. H., Jr. **The Effect of Penicillin on Acute Rheumatic Fever and Valvular Heart Disease.** *New England J. of Med.* 1959, Jan. 15, v. 260, No. 3, 101–12, 7 figs. [24 refs.]

This article deals with a principle which may be important in the treatment of acute rheumatic fever—whether or not salicylates or cortisone should be supplemented by intensive antibacterial (penicillin) treatment, on the supposition that living haemolytic streptococci still play an active role at this stage. According to this view rheumatic fever would not only be a *post*-streptococcal state, but also still in some degree, an acute streptococcal infection. Existing evidence is contradictory and the subject highly controversial.

In this well controlled study of 97 patients with acute rheumatic fever, a 6-week course of intensive penicillin appeared to have no effect on the temperature, joint symptoms, sedimentation rate, C-reactive protein, heart rate, and PR interval—that is, on the acute clinical, laboratory and electrocardiographic manifestations. It did, however, appear to produce a significant reduction in the incidence of valvular heart disease a year later, as judged by the proportion of unalterable valvular lesions present at the end of the experiment as compared with the beginning. There was thus a disparity between the effects on the acute-phase manifestations and those on the endocardial lesions, and this is interpreted as meaning that living streptococci may still be active in the heart valves, but not elsewhere in the body, even after the appearance of symptoms of acute rheumatic fever. On the evidence of this carefully planned experiment, subjective though some of it may be, an intensive course of penicillin may be an important supplement in the treatment of acute rheumatic fever, because of its possible effect on valvular heart disease. *H. Stanley Banks*

JOHNSON, Eloise E., MATHEWS, M. J. & STOLLERMAN, G. H. **The Use of Weekly Oral Doses of Sulfamethoxypyridazine for Rheumatic Fever Prevention.** *J. Pediatrics.* St. Louis. 1959, Apr., v. 54, No. 4, 468–73. [16 refs.]

In an attempt to find an easier and more reliable form of chemoprophylaxis against streptococcal infection in rheumatic children, the long-acting sulphonamide sulphamethoxypyridazine was given to 30 patients in once-weekly doses of 2 or 3 grammes according to weight. The drug was well tolerated except for occasional drowsiness and headache. Blood levels of sulphonamides 24 hours after the weekly dose ranged from 6·5 to 24·6 mgm.% in all of 63 samples tested: after 5 days in 42 of 43 blood samples the mean level was 2·8 mgm.%. Of 57 samples studied after 7 days, 29 showed more than 0·5 mgm.%, 21 showed traces, and 7 showed no detectable sulphonamide. There was no evidence of cumulative levels. No patient acquired group A haemolytic streptococci during the period of prophylaxis. The authors feel this use of drug is a promising one and should be further investigated.
*A. B. Christie*

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# Heart Disease

KARVONEN, M., ORMA, E., KEYS, A., FIDANZA, F. & BROZEK, J. **Cigarette Smoking, Serum-Cholesterol, Blood-Pressure, and Body Fatness. Observations in Finland.** *Lancet.* 1959, Mar. 7, 492–4. [11 refs.]

The evidence suggests that there is a higher mortality from heart disease among cigarette smokers than among non-smokers [this *Bulletin*, 1958, v. 33, 753], but it is not clear whether this a cause-and-effect relationship or whether smokers differ from non-smokers in respect of other factors which are directly related to the development of the disease. The incidence of ischaemic heart disease is high in Finland—particularly in East Finland —and samples of the Finnish population were, therefore, examined and the data obtained for serum-cholesterol, blood pressure and body fatness were studied in relation to smoking habits. A number of small communities were chosen to represent the rural populations of East and West Finland. Men aged 20–59 years were selected for examination, with the exclusion of civil servants, temporary residents and those known to be ill; the majority were farmers or timber workers. The samples are believed to be representative of the men of these ages in the 2 areas concerned. A group of men was also examined in Helsinki; one-half were members of the fire department and one-half were volunteers recruited from members of a local professional and business men's club. It is recognized that the data obtained from this group may be biased.

The numbers of men classified as pipe, cigar or occasional smokers were too small for useful statistical analysis and these, together with a heterogeneous group of ex-smokers, have been excluded. The data reported relate, therefore, to those obtained from regular cigarette smokers and from non-smokers.

The results show that the proportion of heavy cigarette smokers was highest in East Finland. In all areas and at all ages—with the single exception of men aged 50–59 years in West Finland—the serum-cholesterol levels were higher among the cigarette smokers than among the non-smokers and many of the differences were substantial (*i.e.*, more than 20 mgm. per 100 ml.). The differences were, moreover, greater, the greater the amount smoked. They could not be attributed to differences in physical activity, since the proportions of men employed in heavy manual work and in light work showed no systematic differences. In all regions and at nearly all ages the systolic and diastolic blood pressures were lower among the smokers than among the non-smokers. The differences were small but, in sum, statistically significant. In the rural areas, the smokers tended to be thinner than the non-smokers, but no difference was observed in Helsinki, where the men were, in general, fatter than in the rural areas.

The observed differences may indicate that habitual cigarette smoking causes a rise in serum cholesterol or that the kind of person who takes up smoking is also the kind that tends to develop an elevated serum cholesterol. *Richard Doll*

# Cancer

LEGUÉRINAIS, J., DENOIX, P. F. & MAUJOL, L. A propos de l'évolution de la mortalité par cancer dans le monde. **[Evolution of Cancer Mortality in Different Countries]** *Bull. Inst. Nat. Hyg.* Paris. 1958, July–Sept., v. 13, No. 3, 621–41, 2 graphs.

The increase in the annual number of deaths attributed to cancer is striking. It does not follow, however, that the risk of dying of cancer at a given age has increased; and it is, in fact, probable that the risk has scarcely altered since the beginning of the century. At least 4 factors are responsible for creating the appearance of an increase: (1) increased precision in the diagnosis of cancer, (2) a large decrease in the number of deaths certified as due to senility or unknown cause, (3) modifications in the systems of death certification, with greater preservation of medical secrecy, and (4) the progressive increase in the average age of the population. One factor operating in the opposite sense is improvement in the treatment of cancer with a consequent reduction in fatality.

The present report is confined to an analysis of the changes in crude cancer mortality among women between 1901 and 1955. Data are given separately for 14 countries for cancer of (1) all sites, (2) the uterus, (3) the genital organs and (4) the breast. For the main part, figures are calculated for 5-year periods, but for some of the countries the data are not available in the early years or in the last 2 years. Between 1901 and 1955 the mortality for all sites increased in all countries. The difference between the highest and the lowest mortality rates remained much the same (2·7 : 1 and 2·3 : 1), but the relative position of the countries altered. The annual rate of increase varied from 0·32% in Japan and 0·59% in Switzerland to 1·66% in Australia and 2·54% in New Zealand. In 1953 the highest rates were recorded in Denmark and Scotland (183 and 182 per 100,000) and the lowest rates were recorded in Spain and Japan (79 and 78 per 100,000). It is thought that these increases are artificial and due to the factors discussed previously.

Data for cancer of the uterus show a similar range of differences between countries. Most countries show a decrease in mortality (as much as 0·48% annually in England and Wales and, in the last 23 years, 0·83% in the U.S.A.). In Norway and Denmark, however, there has been a substantial increase in mortality. In 1951–5 the highest rate was recorded in Denmark (22·7 per 100,000) and the lowest was recorded in Spain (9·4 per 100,000). In 6 countries, for which data have been given for all genital organs, there has been a substantial increase in mortality—which must reflect an increase in deaths attributed to cancer of the uterine adnexa and of the external organs.

The range of mortality for cancer of the breast was very much greater than for the other types of cancer (8·6 : 1 in 1901–5 and 10·6 : 1 in 1951–5). In 1951–5 the highest mortality was recorded in England and Wales (36 per 100,000) and the lowest in Japan (3·4 per 100,000). In all countries there has been a steady increase—varying from 1·5% annually in Japan to 4·9% in Norway. The reason for the increase is not clear.

*Richard Doll*

KIRCHOFF, Helen & RIGDON, R. H. **Cancer of the Lung—the Sex Ratio. A Review of the Problem.** *Texas Reports on Biol. & Med.* 1959, v. 17, No. 1, 29–48. [147 refs.]

The authors review data on the sex ratio of 17,609 patients with lung cancer reported between 1878 and 1957. They point out that the ratio of the crude numbers reported in autopsy and hospital admission series may give a false impression, because the numbers of autopsies carried out and the numbers of hospital admissions are often unequal in the 2 sexes. They conclude that the sex ratio has probably increased during the period that the mortality from lung cancer has risen, but the extent of the increase is unlikely to be as great as has sometimes been thought. In their opinion " It would appear from this review that the male–female ratio of lung cancer was approximately 3 or 4 to 1 in 1900 and 5 or 6 to 1 in 1955 ".

*Richard Doll*

CORNFIELD, J., HAENSZEL, W., HAMMOND, E. C., LILIENFELD, A. M., SHIMKIN, M. B. & WYNDER, E. L. **Smoking and Lung Cancer: Recent Evidence and a Discussion of some Questions.** Reprinted from *J. Nat. Cancer Inst.* 1959, Jan., v. 22, No. 1, 173–203, 1 fig. [85 refs.]

In 1957 a study group appointed by the National Cancer Institute, the National Heart Institute, the American Cancer Society and the American Heart Association examined the scientific evidence on the effects of tobacco smoking on health and concluded that " The sum total of scientific evidence establishes beyond reasonable doubt that cigarette smoking is a causative factor in the rapidly increasing incidence of human epidermoid carcinoma of the lung ". Concurrently the Medical Research Council of Great Britain [this *Bulletin*, 1957, v. 32, 960] concluded that the " most reasonable interpretation " of the evidence was one of direct cause and effect.

To the evidence then available there have since been added in confirmation data from 3 other retrospective studies on men (France, Japan and the U.K.), 2 more retrospective studies on women (U.S. and U.K.) and a third large prospective study (U.S.) which included 200,000 veterans observed for 2½ years and which duplicated closely the findings of the HAMMOND and HORN [*ibid.*, 1958, v. 33, 753] and DOLL and HILL [*ibid.*, 1957, v. 32, 145] studies. To other aspects of the problem additional data have been published on the more frequent occurrence of hyperplastic and metaplastic changes in the lungs of smokers as compared with the lungs of non-smokers, additional confirmations have been obtained on the induction of cancer of the skin in mice painted with tobacco-smoke condensates and progress continues on the isolation and identification of chemical constituents in tobacco smoke, including compounds of the carcinogenic polycyclic type.

This growing and consistent body of evidence has had no noticeable effect upon the viewpoint of a small but important group of individuals who would deny a causal role of cigarette smoking in cancer of the lung. In this paper the present group of authors review the various criticisms in the light of new evidence, pointing out where already recorded facts directly answer some of them and where further research is especially required. They consider, for instance, such questions as the contribution of improving diagnostic measures, the recorded urban–rural differences and the sex disparity in lung cancer mortality, the possible selective factors in the special groups that have been retrospectively or prospectively studied, the conflicting evidence on inhaling and the results of animal experiments. Taking the criticisms and the evidence generally into account they discuss the possible interpretations and accept the causal as best fitting all the known facts. Against the constitutional hypothesis they place the following points: (a) changes in lung cancer mortality over the last half century, (b) the carcinogenicity of tobacco tars for experimental animals, (c) the existence of a large effect from pipe and cigar tobacco on cancer of the buccal cavity and larynx but not on cancer of the lung, and (d) the reduced lung-cancer mortality among discontinued cigarette smokers. No one of these considerations is perhaps sufficient by itself to counter the constitutional hypothesis, *ad hoc* modification of which can accommodate each additional piece of evidence. A point is reached, however, when a continuously modified hypothesis becomes difficult to entertain seriously.

The summary of their conclusions is as follows:—

" The magnitude of the excess lung-cancer risk among cigarette smokers is so great that the results can not be interpreted as arising from an indirect association of cigarette smoking with some other agent or characteristic, since this hypothetical agent would have to be at least as strongly associated with lung cancer as cigarette use; no such agent has been found or suggested. The consistency of all the epidemiologic and experimental evidence also supports the conclusion of a causal relationship with cigarette smoking, while there are serious inconsistencies in reconciling the evidence with other hypotheses which have been advanced. Unquestionably there are areas where more research is necessary, and, of course, no single cause accounts for all lung cancer. The information already available, however, is sufficient for planning and activating public health measures."

[This is an extremely readable review which should be studied in full.] *A. Bradford Hill*

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GYURECH-VÁGÓ, E. & SCHERRER, M. Über die Beziehungen zwischen chronischer Bronchitis und Bronchuskarzinom. **[Relationship Between Chronic Bronchitis and Bronchial Carcinoma]** *Schweiz. med. Woch.* 1958, Nov. 8, v. 88, No. 45, 1132–6, 5 figs. [41 refs.]

The causes of lung cancer, among which smoking takes first place, are not wholly elucidated. Many authors consider that the disease results from the interaction of several factors and some have suggested that tuberculosis or chronic non-specific inflammatory processes predispose to the development of the disease. The literature on this point is, however, contradictory.

In the present study, 126 patients with bronchial carcinoma were questioned about their previous respiratory illness and were subjected to tests of respiratory function. 81 patients (64%) gave a history of various lung disorders—33 (26%) had relapsing pneumonia, previous pulmonary tuberculosis or pleurisy, a few had experienced trauma to the thorax; the remaining 48 (38%) had symptoms of a chronic relapsing bronchitis which had persisted for at least 4 years before the diagnosis of cancer was made. Of these 14 (11% of the total) had required treatment for bronchial asthma.

Lung function tests showed an average vital capacity for the cancer cases of 94% of the " standard " value against 123% for a group of subjects with healthy lungs. Measurements of residual volume showed a very wide scatter of from 50% to 300% of the theoretical value, due to the conflicting effects of a space occupying lesion and of an obstructive lesion producing emphysema. Evidence of bronchiolar obstruction was obtained in 107 patients (85%) by the 1-second expiration volume test and evidence of bronchospasm was obtained in 85 patients (65%) by the " Aleudrin test ". The bronchitis and bronchospasm were not secondary to the tumour because in most cases they antedated the appearance of the tumour; in 8 cases in which the tumour was removed the broncho-asthmatic obstruction to expiration remained unaltered. Smoking histories were obtained for 110 patients. Of these 100 were moderate or heavy smokers. Of the 10 patients who smoked occasionally or never, chronic asthmatic bronchitis was revealed in 9 by the history or by pulmonary function tests.

These data, it is suggested, imply an aetiological relationship between bronchial asthma or chronic asthmatic bronchitis and bronchial carcinoma.

*Richard Doll*

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STOCKS, P. **Air Pollution and Cancer Mortality in Liverpool Hospital Region and North Wales.** *Internat. J. Air Pollution.* London. 1958, Oct., v. 1, Nos. 1/2, 1–13, 2 figs.

A field study of cancer incidence in North Wales and the Liverpool Hospital Region was started in 1952 and measurements of the degree of atmospheric pollution in various parts of the area were begun in 1954. By the winter of 1956, 23 instruments were installed at sites chosen to provide samples representative of places with different population densities and the present report relates to the total amount of smoke and the amount of hydrocarbons in the air at these stations between October 1956 and April 1957. Of the total instruments, 17 were sited in localities with population densities varying from 0·1 to 28·9 persons per acre; 3 were sited in the Mersey Tunnel to measure the effect of dense road traffic, 2 in bus and motor garages and 1 inside an office.

Both the smoke and the hydrocarbon content of the air (as measured by the benzpyrene, benzperylene, pyrene and fluoranthene contents) was clearly related to the population density of the area. The average smoke concentration varied from 1·7 mgm./100m³ in the Conway valley to 62·4 mgm./100m³ at one site in Liverpool; the benzpyrene content varied similarly from 0·1 $\mu$gm./100m³ of air to 6·75 $\mu$gm./100m³.

Measurements in the Mersey Tunnel showed that the air taken in by the ventilating system was less polluted than the average street air of Liverpool. The smoke concentration increased up to nearly 5 times at a junction in the tunnel where cars were often held up; but the concentration of hydrocarbons in the smoke was less than in normal street pollution, so that although the maximum smoke concentration rose to 3½ times that in street air, the concentration of hydrocarbons was either less than or only slightly more than in street air. Measurements of air inside and outside a garage for diesel buses and a garage for ordinary motors showed some slight increase of smoke in the motor garage but the differences recorded in the hydrocarbon contents were too small to be certain that they were significant.

Correlation between the Standardized Mortality Ratios for (1) lung cancer and for (2) intestinal cancer in the 15 local authority areas, with (a) population density and (b) smoke concentration, failed to show any substantial correlation in the case of intestinal cancer. In the case of lung cancer, both correlation coefficients were significant (0·830 and 0·826). Population density and smoke concentration were, however, themselves closely correlated (0·889) and the partial correlations with one factor and the other held constant were reduced to 0·371 (population density) and 0·346 (smoke concentration). The partial correlation coefficients between lung cancer and the individual hydrocarbons—benzpyrene, benzperylene, pyrene and fluoranthene—were 0·28, 0·48, 0·45 and 0·36 respectively. ". . . it appears that, whilst smoke is an important contributor to the excess of lung cancer found in large towns, other factors are also contributing to this, such as the rather higher rate of heavy cigarette smoking in towns."

*Richard Doll*

COMMINS, B. T. **Polycyclic Hydrocarbons in Rural and Urban Air.** *Internat. J. Air Pollution.* London. 1958, Oct., v. 1, Nos. 1/2, 14–17.

This report describes the method by which the polycyclic hydrocarbon content of the air was measured in the course of the British Empire Cancer Campaign's special survey described by STOCKS [see above]. The smoke samples were collected on filter papers in urban and rural districts of North Wales, Cheshire and Lancashire and the weight of smoke assessed by reflectance measurements. The smoke papers were extracted in acetone and the extract was reduced to dryness and redissolved in cyclohexane. The hydrocarbons in this extract were separated chromatographically on a column of activated alumina and the amounts of each hydrocarbon determined in bulked eluates by ultra-violet spectrophotometry. The amounts of pyrene, fluoranthene, 3 : 4-benzpyrene and 1 : 12-benzperylene were determined for each of the 23 sites sampled and the results expressed as parts of hydrocarbons per 100,000 parts of smoke and $\mu$gm. of hydrocarbon per 100 cu. metres of air. The concentration of the hydrocarbons was much lower in rural areas than in urban.

Pyrene is measured without much difficulty, as it exhibits a strong peak at 335 m$\mu$. Fluoranthene has a strong absorption at 287·5 m$\mu$ but the measured amount may contain some 1 : 2-benzanthracene which has an absorption peak close to it and appears with fluoranthene towards the end of the elution. The measurement of 3 : 4-benzpyrene depends upon a weak absorption peak at 403 m$\mu$. This can be masked by other materials present and considerable errors may arise when very small amounts are measured. Large samples of smoke were, therefore, used for analysis whenever possible. The determination of 1 : 12-benzperylene depends to some extent on the amount of benzpyrene measured (both have peaks at 385 m$\mu$) and when errors arise in the measurement of benzpyrene they will be reflected in the measurement of the benzperylene.

*Richard Doll*

GORHAM, E. **On the Correlation of Lung Cancer with Tar in Air Pollution.** *Med. Officer.* 1959, Mar. 26, v. 101, No. 13, 178, 1 fig.

Crude death-rates from cancer of the lung and bronchus were calculated for the years 1950–4 for 53 boroughs in England and Wales. A measure of the atmospheric tar deposit in each of these boroughs was taken from the 27th Report of the Department of Scientific and Industrial Research [this *Bulletin*, 1956, v. 31, 763]. Both measures were transformed to logarithms, to provide more normal distributions and the correlation between them was then calculated. A small, though highly significant, coefficient was found (+ 0·35). The death-rate in the most highly polluted districts is 25–30% higher than that in the least polluted district.

*A. Bradford Hill*

POLYDOROVÁ, Marie. Pokus o stanovení retence tabákového kouře v plicích pomocí membránových filtrů. [ **An Attempt to determine the Retention of Tobacco Smoke in the Lungs by means of Membrane Filters**] *Československ. Hyg.* Prague. 1958, v. 3, No. 7, 421–6, 4 figs. [22 refs.] English summary (6 lines).

Cigarette smoke was aspirated by means of a rotary oil pump through a membrane filter 150$\mu$ thick of pore diameter 0·9$\mu$, the rate of air flow being adjusted to simulate different smoking habits. The amount of smoke retained was determined by weighing the filter before and after use, and the filter was then dissolved in amyl acetate and the deposit was prepared for examination in the electron microscope. Similar preparations were made of smoke exhaled from the lungs. Comparison of 2 sets of results showed that a heavy smoker (more than 15 cigarettes a day) would retain up to 88·7% of the smoke in the lungs, whereas a light smoker would retain 63·4% and an occasional smoker 21·8%. The particle size of the smoke ranged from 0·1 to 0·5$\mu$, and most of the smaller particles were retained in the lungs.

*D. J. Bauer*

SCIARINI, L. J. & MEIGS, J. W. **The Biotransformation of Benzidine (4,4'-Diaminobiphenyl), an Industrial Carcinogen, in the Dog.** I. *Arch. Indust. Health.* Chicago. 1958, Dec., v. 18, No. 6, 521–30, 1 fig. [28 refs.]

After injection of benzidine intraperitoneally into a dog, it is possible to recover from the urine 2 to 9% of the substance unchanged and 25 to 50% in the form of 3-hydroxybenzidine ethereal sulphates. A further 5 to 10% is excreted in the faeces. The amounts of benzidine and of its hydroxylated derivative were determined colorimetrically; the substances were isolated and characterized by chemical analysis and by comparison with proved synthetic preparations.

It has been reported elsewhere that the principal metabolite of benzidine is 3,3'-dihydroxybenzidine, but the presence of this substance in the urine was not recognized; nor was the glucuronide conjugate, which has been demonstrated to be produced with β-naphthylamine derivatives in man.

Benzidine exposure is known to produce bladder cancer in man, but unlike the experience with β-naphthylamine and p-aminophenyl, the administration of the pure product has failed to produce bladder cancers in dogs. It is believed that the major metabolites are likely to be the same in dog and man and the recognition of the principal metabolite in the dog will allow direct studies to be made of its carcinogenic potency.

*Richard Doll*

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## Miscellaneous Diseases

ST. GEORGE-GRAMBAUER, Betty M. **Diseases of Laboratory Mice.** Reprinted from *J. Animal Technicians Ass.* 1958, Dec., 7 pp.

" Among the 481 sick or abnormal mice studied during twelve months in the breeding colony of the Queensland Institute of Medical Research, the commonest conditions found were megacolon (83), chronic inflammation of the lungs (57), *Corynebacterium murium* abscesses of lungs (29) and of liver (12), Tyzzer's disease of liver (21), *Streptobacillus moniliformis* infection (17), hydrocephalus (15), spinal deformity (8), muscle necrosis (6), volvulus (6), intussusception (5).

" Tumours found included mammary adenocarcinoma (10), lymphosarcoma (2), ovarian teratoma (1), ovarian cystadenoma (1). All these were in mice at least six months of age.

" The morbidity was highest in the months of July, August and September when infectious diseases were most prevalent.

" In 78 cases autopsy did not disclose the cause of illness."

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## Dental Hygiene

VERBRAECK, L. La carie dentaire chez les habitants de la cuvette du fleuve Congo. [**Dental Caries in Inhabitants of the Congo River Basin**] *Ann. Soc. Belge de Méd. Trop.* 1958, Oct. 31, v. 38, No. 5, 983–9.

During the years 1947 and 1948 the author carried out dental examinations of 10,120 African adults living in the Congo river basin. Only 1,831 teeth were missing, *i.e.* on the average about one tooth was missing for every 6 individuals. The frequency of dental caries in the different types of teeth was as follows:—

| | |
|---|---|
| Incisors ... ... ... ... ... | 2·7% |
| Canines ... ... ... ... ... | 1·8 ,, |
| Premolars ... ... ... ... ... | 4·5 ,, |
| First Molars ... ... ... ... ... | 6·2 ,, |
| Second Molars ... ... ... ... | 8·7 ,, |
| Third Molars ... ... ... ... ... | 24·0 ,, |

In Léopoldville, Matadi, Kikwit and Coquilhatville a comparison was made, based on examinations in the years 1946, 1947 and 1948, between the caries incidence of the first and second permanent molars in white children, aged about 12–16 years [given as 12–18 in the author's summary], and the incidence in comparable African children. The caries frequency was about 85% in the white children and about 5% in the African children.

*Robert Weaver*

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## Mental Hygiene

HERD, J. A. & SHADDICK, C. W. **Mental Illness. An Analysis of Data recorded by the Mental Welfare Officers in the County of London.** *Med. Officer.* 1958, Oct. 10, v. 100, No. 15, 233–8.

This topical and valuable paper is from the health department of the London County Council where Dr. Herd is the consultant psychiatrist and Mr. Shaddick is the statistician.

It analyses particulars of the 7,630 consecutive cases of mental illness referred to the mental welfare officers during 1956. The London County Council scheme is unique not only by reason of its size but also because of the traditional system by which patients referred to mental welfare officers are normally passed through large and well staffed observation units attached to former poor law general hospitals.

The sources of referral were 861 (11·2%) from psychiatrists or psychiatric hospitals or departments; 3,257 (42·6%) from general medical practitioners; 874 (11·5%) from the wards and 737 (9·7%) from the casualty departments of general hospitals; and 1,901 (25·0%) from non-medical sources such as relatives and the police. There were 6,318 individuals included in the 7,630 referrals as many were dealt with more than once during the year: in 31 cases 5 times or more. The 6,314 individuals discussed comprised 2,650 males and 3,664 females. The only age-group with more men than women was 21–30 with 444 men and 373 women. The rate per 10,000 population at age specific grouping was heaviest at the older ages namely 47·8 for ages 70–80 and 113·8 for age 80 +.

Tables give details of the initial action taken by the mental welfare officers of whom there are 26 covering between them a round-the-clock service. These officers, who are laymen, can remove a patient from his home only when they are satisfied that " he is not under proper care and control, and that there are no relatives or friends able or willing to make appropriate arrangements ". In 1,666 (21·8% of the 7,630 referrals) these conditions were not fulfilled: in 53·6% of the total the patient was admitted to an observation ward and in 19% a Justice of the Peace was called in with a view to direct admission to a mental hospital. It is interesting to note that of the 4,100 admitted to these wards 1,405 were discharged before the 17 days maximum period of detention there allowed by law had elapsed: 1,383 went as voluntary, and 1,100 as certified, patients to mental hospitals. Altogether in 3,419 (44·8%) of the 7,630 referrals " no further care " was " possible or necessary " at the time the investigation came to an end.

The advantages of short-stay accommodation in a " psychiatric emergency bed service " are set out but even better would be an assessment by a psychiatrist in every case in the patient's home or where he is at the time when referrals are made. This procedure already operates in London in the catchment area of the Bexley Hospital and in Essex in that of the unit for the elderly at the Langthorpe Hospital.

[Most of the present procedure will come to an end when the new Mental Health Act becomes operative. When the abstracter was responsible for this work at the London County Council he put forward the proposal that every patient before admission to a mental observation ward should be seen by a psychiatrist. It was not, however, acceptable to the Board of Control because, though enough psychiatrists would be available in London, they would not be throughout the rest of the country and it was thought it would be too confusing to have different legal procedures in London and elsewhere.]

*Allen Daley*

Lowry, D. M. O. **Community Care of the Mentally Ill; Present and Future.** *Med. Officer.* 1958, Oct. 10, v. 100, No. 15, 239–41.

This paper is from the health department of the Battersea Metropolitan Borough Council and the divisional medical office of the London County Council.

It describes with lurid detail the case history of a coloured woman, married with one child, who developed paranoid schizophrenia and eventually had to be certified as insane. But, after 23 days she was regraded as a voluntary patient whereupon she discharged herself and proceeded to create further disturbances at home. The hospital had not notified the local authority of her discharge. After she had set the house on fire she was again certified and re-admitted to hospital where she remained this time for 11 weeks when she was released on trial in the care of her husband who, however, was away from home for 12 hours a day.

After another 4 weeks at home she was re-admitted once more and there the story ends.

The case illustrates well how disturbing such a person can be to her family and neighbours: in this case it was complicated by the presence of a young child who had to be taken " into care " by the Children's Officer whenever the circumstances warranted.

The lesson drawn from this case is that there is need for more consultation between mental hospitals and the local authorities responsible for community care and in particular that on discharge of a patient the hospital should give all relevant information to the local authority. In this instance all that was done was to advise the patient to visit a psychiatric out-patient clinic which, as might be expected, she never did.

Macmillan of Nottingham (*Lancet*, 1956, v. 2, 1094) is quoted to the effect that the only satisfactory solution is an integrated hospital-local authority service in which the hospital can use the social workers of the local authority and the local authority can use the medical staff of the mental hospital. The dangers of premature discharge of patients especially if there is no prior consultation about after-care are well set out.

[This is an intensely practical paper which shows what may happen if we move too quickly in the direction of treating mental in exactly the same way as physical illness.]

*Allen Daley*

Hargreaves, G. R. **Psychiatry and the Public Health.**

This book was reviewed on p. 594.

# Occupational Hygiene

*In this section the abstracts are arranged as far as possible in the following order: General; Mining and Dust Diseases; Poisoning due to Metals, Solvents and Other Substances; Skin and Other Affections; Radio-Active Substances; Other Conditions; Occupational Psychology*

MINISTRY OF LABOUR & NATIONAL SERVICE. **Annual Report of the Chief Inspector of Factories on Industrial Health for the Year 1957** [MCCULLOUGH, T. W.]. Cmnd. 558. 50 pp. 1958. London: H.M. Stationery Office. [3s.]

In the past the Annual Report of the Chief Inspector of Factories has consisted of a single volume covering all aspects of the work of the Inspectorate, but it has been decided to publish a separate report dealing with industrial health. Brief references to major matters in this field appear in the main Annual Report, but the more complete information now appears in this separate report on industrial health.

During the year under review a preliminary draft of special regulations concerning ionizing radiations was published, and at the end of the year a large number of observations and suggestions were being closely examined. The draft regulations are concerned with the use of sealed sources, and they seek to safeguard the health of workers by adequate shielding or, where that is not practicable, by limiting the time of exposure so that the dose of radiation received is below the maximum permissible level.

A draft of regulations dealing with work in compressed air was also published during the year, and the regulations came into operation in April 1958.

On the advice of the Industrial Health Advisory Committee 2 industrial health surveys were made. One of these, carried out in Halifax, was aimed at determining the industrial health situation in a typical industrial town, the extent to which industrial health services were needed in the town, and how they could best be organized to suit the conditions existing. An abridged version of the report on the survey has been published.

The second survey was made in the pottery industry with the object of examining health hazards, including possible hazards less well recognized than lead poisoning and pneumoconiosis. By the end of 1957 all the 298 establishments coming within the scope of the survey had been visited.

Early in the year the Minister appointed a committee to inquire into precautions against anthrax.

The third interim report of a committee of the cotton industry on dust in card rooms indicates that the Shirley Pressure-Point System provides a practical method of removing the dust from carding engines as near as possible to its point of origin, so that it does not enter the card rooms.

3 committees have continued the investigation and consideration of dust and fume problems in the metal founding industry. The problems of various operations are being investigated, but it is remarked that conditions in all types of foundries can be improved beyond measure by scrupulous attention to general cleanliness, ventilation and segregation of processes.

Developments towards the reduction of health hazards are reported in certain lead processes, in fibre-glass moulding, in applying crease-resisting finish to cloth, and in the ventilation of crane cabins in steelworks.

The report contains tables giving the usual particulars of cases of notifiable industrial poisoning or disease, and of cases of industrial dermatitis notified voluntarily. In the text accounts are given of many of these cases, and of the conditions under which they arose. *T. Bedford*

REJSEK, K. Die Berufskrankheiten des Gesundheitspersonals. [**Occupational Diseases of Medical Personnel**] *Santé Publique.* Bucharest. 1958, v. 1, No. 1, 73–88. [30 refs.]

In this long paper there is an account of occupational disease in medical personnel based on observations in Czechoslovakia. The most important of these diseases is tuberculosis and the data on this are analysed by age, length of service and type of the tuberculosis institution. Particular emphasis is placed on the high incidence of tuberculosis in those who are engaged in autopsies, and the causes of this frequency of infection are discussed. Infective and serum hepatitis are also occupational diseases which occur in medical and nursing staff by infection from patients and in laboratory workers through contact with infected tissues or apparatus. These infections are also discussed with stress on the importance of better technique and greater personal care. The effects of exposure to X-rays, whether as dermatitis or changes in the blood picture, have been by no means infrequent and have often been due to carelessness or ignorance. In recent years skin diseases particularly eczema and allergic conditions some of which are due to sensitivity to antibiotics, have become more frequent.

The prevention of medical occupational disease by better techniques and training of personnel is stressed. *M. E. Delafield*

ROYAL SOC. PROMOTION HEALTH J. 1959, Mar.–Apr., v. 79, No. 2, 154–69, 4 figs. **The Health of Workers in Non-Industrial Premises. (a) The Gowers Report** [BACON, Alice], 154–6. **(b) The Forgotten Army** [WATTLEWORTH, W. H.], 156–67. Discussion 167–9.

These 2 papers were presented at a Sessional Meeting of the Royal Society for the Promotion of Health in January, 1959. The first of these deals with the inadequacy or lack of existing legislation for the protection of certain categories of non-industrial workers in regard to their safety at work and their health and welfare. The Gowers Committee whose final report was issued in 1949 made recommendations in respect of these categories which are outlined in this paper. The groups which were considered were workers in (a) shops and offices, (b) hotels, restaurants and catering establishments, (c) backstage of theatres and (d) transport. "The conclusion reached by the Committee was that these workers—over ten million of them, working sometimes in dreadful conditions, particularly in offices and backstage of theatres—should have legislation to give them some measure of protection." In the second paper entitled *The Forgotten Army* the author deals fervently with the inadequacy of legislative protection for over 10 million non-industrial workers classified by the Ministry of Labour and National Service in 1958 as professional and financial; transport and communications; distributive trades; local government; and national government. "This large section of the working population receives less favourable treatment than industrial workers" and "the majority are allowed to work under deplorable and overcrowded conditions in makeshift attics high above the street, in underground rooms, and in insanitary buildings . . . ." This statement is to some extent supported by a considerable description of the author's observations as Chief Public Health Inspector, Liverpool, of environmental conditions in offices and other places in which non-industrial workers are employed. Although it has been possible to secure improvements in working conditions in certain directions these conditions are often by no means satisfactory. "The non-industrial worker has a right to expect healthy and safe working conditions, and if it is necessary to secure these by legislation then the necessary mandatory powers should be provided without undue delay." *M. E. Delafield*

GRANDJEAN, E. Physiologische Untersuchungen über die nervöse Ermüdung bei Telephonistinnen und Büroangestellten. [**Physiological Investigations of Fatigue in Female Telephonists and Office Workers**] *Internat. Ztschr. f. Angewandte Physiol.* 1959, v. 17, No. 5, 400–418, 11 figs.

The results of investigations of fatigue described in this paper were carried out for a period of 4 weeks on 13–15 female telephone workers and on 14 office workers. The tests applied before and after a work shift to study the psychophysiological functions were tests of flicker fusion frequency, equilibrium movements, optical reaction time, calculating performance, accuracy of cancellation of letters (Bourdon test), manual skill and finger tremor. These tests are described shortly. The results of the investigations and their statistical examination are very fully described with a number of figures.

In the telephone worker group highly significant alterations after the work period were demonstrated in flicker fusion frequency and in manual skill. Less significant changes were found by the other tests except that there was (1) no significant change in the calculating performance test and (2) in the Bourdon test of speed of cancellation of letters a statistically highly significant decrease in the time taken was determined. In comparison with these findings those in office workers were similar but the changes observed were much less important. The difference between the 2 groups of workers was most marked in the optical reaction time and the flicker fusion frequency.

*M. E. Delafield*

GOETHE, H., RINCK, G. & GUDMUNDSSON, G. Erkrankungen in der deutschen Hochseefischerei mit Berücksichtigung des Gebisszustandes. [**Sickness in German Deep Sea Fishermen with reference to Dentition**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 1, 57–66. [11 refs.]

In a previous paper an account was given of the medical care provided by the welfare and supply vessels which accompany fishing fleets [this *Bulletin*, 1959, v. 34, 260].

The present paper contains a description of the various sea areas which are fished over by cutters, luggers and steamers, the numbers of men employed and the conditions under which the fishermen work. This introduces an account of the chief diseases of the fishermen during 1950–5 for which medical care was provided by the 2 welfare vessels. A table sets out the numbers of cases derived from the medical records of personnel on steamers and luggers. The most important cause of disability was accidents, which accounted for 30·6% of all disabilities in the steamers and 13·6% in the luggers. The next most numerous disabilities in the aggregate of both types of vessel were septic conditions of the hand (12·9%), diseases of teeth, mouth and jaw (10·5%) and diseases of the digestive tract (10%). These conditions are described and discussed. An interesting state well known to the fishermen and called "thick head" (*dicker Kopf*) is mentioned. It is said to be due to a hypervitaminosis by vitamins D and A from indulgence in tunny fish liver. The symptoms of 6 men who were severely affected were intense headache, vomiting and marked muscular weakness with pains in the large joints. All these men had facial oedema and their urine was grass-green in colour.

There is a detailed account of the dental state of a group of nearly 500 lugger fishermen in whom dental disability is particularly high. Tables give particulars of the chewing capacity (measured by the GONTER method) and the percentages of missing and carious teeth and other dental abnormalities. Gingivitis and parodontal infection were very frequently found presumably due (1) to bad dental care as many of the men never brush their teeth when at sea, (2) excessive use of tobacco, and (3) insufficient vitamin C in the diet. *M. E. Delafield*

FRIEMANN, W., OVERHOFF, W. & WOLTER, J. R. Augenerkrankungen in der Industriefischerei. [**Diseases of the Eye in the Fishing Industry**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 1, 1–56, 54 figs. (10 coloured). [Numerous refs.]

This is a long and detailed paper with many illustrations and numerous references in which the eye diseases in workers engaged in the herring fishery industry are considered from the points of view of their character and causation. Since 1951 the fishing particularly for immature herrings but also for sand eels which are then converted into fish meal used as animal food has developed to a great extent. Eye diseases in those workers who come into close association with masses of fish have become frequent. These take a form which ranges from a transitory conjunctivitis to severe keratitis with permanent loss of vision.

Some particulars are given of the fish, the fishing cutters, methods of fishing, areas where fishing is done and the fishing season. The growth of this fishing in Germany and elsewhere is illustrated by stating the weight of the catch in recent years. Comments are made on the unhygienic conditions in the fishing vessels and there is a long description with photographs of methods in use for landing the catch which is already in varying stages of decomposition. It is in landing the catch that the workers are most exposed to irritant spray from the wet fish. There are 3 clinical accounts of men whose eyes were affected as a result of exposure to the spray.

It was believed that the irritant substance was one of the organic amines produced in the decomposition of fish proteins and in a very long series of experiments on rabbits it was found that trimethylamine was intensely irritant. The early instillation of 0·5% cortisone solution after the introduction of the trimethylamine greatly lessened the irritant effect. The results of these experiments are described at length with photographs of the macroscopic changes resulting from the instillation of trimethylamine. Almost half the paper is devoted to an account with many photographs of the degenerative and regenerative histological changes which were found in the tissues of the eyes of the animals.

There is a summary of a number of changes that are recommended to be made in the fishing boats and in methods of unloading. The workers should if possible wear protective goggles and skilled ophthalmic care should be immediately available to provide treatment and if necessary assure early cortisone administration.

*M. E. Delafield*

Bugyi, B. Coniomicosi dei lavoratori del riso. [**Coniomycosis of Rice Workers**] *Med. d. Lavoro.* 1958, May, v. 49, No. 5, 368–75, 5 figs. [24 refs.] English summary.

From the State Polyclinic at Csepel (Budapest) the author describes a lung condition arising in a factory making cellulose from rice straw. The condition occurred in a sector where the atmosphere was very dusty and the workers complained of cough, difficulty of respiration and sometimes dyspnoeic attacks, and frequent slight blackish expectoration, but fever, cyanosis or cardiac attacks did not occur and the condition was not bad enough to cause absence from work.

On chest X-ray about one-half of the patients showed hilar enlargement with a tendency to reticulation, and one-third of the patients hilar enlargement with greatly increased lung markings especially at the bases often with slight nodular or micronodular non-homogeneous shadows like cotton wool or snow-flakes, close to the bronchi in the mediobasal areas. Sometimes these shadows were massed together resembling silicotic fibrosis. These radiological changes did not alter after several weeks' absence from work, but regressed if the patient was removed for a longer time. No case was [apparently] found with a shorter history of dust inhalation than 3 years.

Chemical examination of the dust showed a surprisingly high free Si content (80·5% of the ashed residue) and microscopically there were numerous sharp-pointed particles quite capable of causing microtrauma of the air-passages which could then become infected with bacteria or fungi. *Aspergillus niger* was present in the dust in quite large numbers and was also found in the sputum along with *Penicillium glaucum.*

The author considers that this syndrome is an occupational disease, the following factors all contributing to it: (1) high free silica content of the rice straw dust; (2) sharp-pointed dust particles; (3) fungi especially *Aspergillus niger* and *Penicillium glaucum*; (4) the high dust content of the factory, where because rice straw dust was previously considered innocuous no special anti-dust precautions had been taken. He states that it is impossible to decide which of these factors is the most important and calls this occupational disease a coniomycosis.

[No details are given of the numbers employed or affected.] *W. K. Dunscombe*

Halen, R. J. **A Comparison of Railroad and Steel Mill Lost Time Cases.** *J. Occupational Med.* Chicago. 1959, Apr., v. 1, No. 4, 203–6.

Storlazzi, E. D. **Hygiene of Welding in U.S. Naval Shipyards.** *Arch. Indust. Health.* Chicago. 1959, Mar., v. 19, No. 3, 307–11.

In U.S. Naval Shipyards 6,000 workmen are employed as welders and burners in the construction and repair of ships. These men are intimately exposed to the inhalation of a variety of metal fumes and gases.

The chest X-rays of all welders, burners and shopfitters taken at the Boston Naval Shipyard during the year 1957 were scrutinized. The series comprised 1,083 men, who had been employed in these occupations from 6 to 41 years; average approximately 18 years. The following cases were discovered:

| Condition | Cases No. |
|---|---|
| Primary healed tuberculosis | 2 |
| Pleural thickening (apical) | 1 |
| Pulmonary fibrosis | 1 |
| Healed pleurisy (basal) | 2 |
| Increased bronchovascular markings | 1 |
| Healed adult tuberculosis | 4 |
| Multiple pulmonary calcification | 1 |
| Nonmalignant pulmonary tumor | 1 |
| Intrapulmonary hemorrhagic nodule | 1 |
| Active tuberculosis | 1 |

The conclusion is that the respiratory hazards of welding and burning in this establishment have been almost eliminated by strict application and enforcement of modern methods of industrial hygiene.

*A. Meiklejohn*

MILIC-EMILI, G. & PETIT, J. M. Il limite alla ventilazione polmonare durante l'esercizio muscolare negli insufficienti cardio-respiratori. [**The Limits of Pulmonary Ventilation during Exercise in Patients with Cardio-Respiratory Insufficiency**] *Med. d. Lavoro.* 1959, Mar., v. 50, No. 3, 175–80, 3 figs. [10 refs.]

The English summary appended to the paper is as follows:—

"In subjects with cardio-respiratory disability due predominantly to impairment of the ventilatory function, pulmonary ventilation during exercise is limited by mechanical insufficiency of the ventilatory apparatus. In this case, the highest values of ventilation during exercise are of the same order as MBC values.

"On the other hand, in patients with impaired respiratory exchanges and circulation, the limit to ventilation during exercise is not conditioned by mechanical insufficiency, but is reached when the increment of $O_2$ introduced into the organism is equal to the increment of the $O_2$ consumed by the respiratory muscles. Thus a further increase in ventilation would lead to a decrease of the $O_2$ available for the non-ventilatory functions. In this case, MBC values exceed the highest ventilatory values found during exercise."

SADOUL, P., METZ, J. & SAUNIER, C. Intérêt des épreuves fonctionnelles dans le diagnostic et le traitement des bronchites chroniques. [**Functional Tests in the Diagnosis and Treatment of Chronic Bronchitis**] Reprinted from *J. Français Méd. et Chirurg. Thoraciques.* 1957, v. 11, No. 6, 664–80, 5 figs. [27 refs.]

A group of 234 carefully selected patients with chronic bronchitis were classified into 3 sub-groups according to the degree of dyspnoea: I, non-breathless "coughers"; II, moderately dyspnoeic, and III, grossly dyspnoeic. This classification was supported by lung function measurements and tests as follows: mean vital capacity, normal, 4·266; I, 4·450; II, 3·735; III, 3·050 litres: mean one second timed vital capacity, N, 3·287; I, 3·120; II, 1·990; III, 1·215 litres: mean residual volume as percentage of total vital capacity, N, 26·9; I, 28; II, 36, III, 47.

The proportion of patients examined who reacted to the broncho-constrictor drug acetylcholine and the broncho-dilator drug aleudrine increased from normal to group III. *M. L. Thomson*

GOLDBLATT, M. W. **Occupational Carcinogenesis.** *Caribbean Med. J.* 1958, v. 20, Nos. 1/4, 81–91. [Numerous refs.]

A general review and discussion.

SUTTER, R. A. **The Nurse's Role in Health Maintenance and Accident Prevention.** *Indust Med. & Surgery.* Miami. 1959, May, v. 28, No. 238–45, 3 figs.

MIURA, T. & KIMURA, K. [**Hazardous Dust in Foundry Work. Studies on the Dust Control (Rep. IV)**] *J. Sci. of Labour.* Tokyo. 1959, Mar., v. 35, No. 3, 241–51, 8 figs. [20 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"The dust problem of the foundry is recognized in the larger plants, but may not be in the smaller ones. The lack of dust control in the smaller plants is not necessarily due to the lack of interest but rather to the fact that they have not been reached by industrial hygiene engineers to explain the importance and benefits to be derived from an adequate dust control program.

"Most foundries in Japan are small having less than 50 workers and less than 1,500m² floor, therefore effective dust control programs are not developed.

"Siliceous dust suspended in the air was investigated in 12 foundries. The dust concentration was measured by means of 'Roken Dust Counter,' 'Filter Paper Dust Sampler', the thermal precipitater, the impinger and the electric precipitater.

"The dust concentration during moulding of the large casting was higher than the small one.

"The atmospheric dust concentration in the shake out and core knockout in several foundries were often above 5,000 dust particles per cc and the amount of the atmospheric dust was large in excess of the permissible level.

"The air borne dust concentration in the blast cleaning, grinding, chipping of casting were often high concentration, therefore the dust control program of the shake out and core knockout and of the casting polishing is necessary.

"The amount of free silica in the materials of casting sand and the deposited dust in foundry rooms was analyzed by the phosphoric acid method or X-ray spectrometry and the amount of free silica of deposited dust was 40–85%."

HAMLIN, L. E. **Siderosis: Additional Observations over a Period of Eight Years on Sixty-Nine Foundry Cleaning Room Employees.** *J. Occupational Med.* Chicago. 1959, Feb., v. 1, No. 2, 79–93, 13 figs.

In 1950 HAMLIN and WEBER [this *Bulletin*, 1950, v. 25, 1025] reported on 69 workmen employed as burners and grinders in factories of the American Brake Shoe Company, Chicago. Serial radiographs had been observed over a period of 16 years; 67% of the men developed nodular shadows in less than 10 years. The processes involved exposure to high concentrations of iron dust and to slight amounts of free silica. They concluded that the condition was a benign form of pneumoconiosis—siderosis—due to the retention of radio-opaque iron particles within the lungs. While not altogether excluding the possibility that in some cases the silica might have been a factor, they emphasized that the amount of $SiO_2$ was well below the safe permissible limits and that most of the particles were above the respirable limit of $10\mu$. They were unable to offer precise pathological proof of their contentions as no fatal case had occurred.

These 69 workmen, who have since been subject to annual radiographic examination, have now been observed for a further period of 8 years. The after-histories are summarized as follows:

Present Status of 69 Cleaning Room Employees Observed From 1949 to 1957.

| | | |
|---|---|---|
| Number of men still working | | 41 |
| At original jobs (grinding, burning, etc.) | 28 | |
| At comparable jobs (cleaning room, machine shop) | 4 | |
| At lighter nondusty jobs | 5 | |
| As foremen | 4 | |
| Number of men retired | | 17 |
| Number of men who have terminated employment | | 5 |
| Number of men who have died | | 5 |
| Number of men absent because of pulmonary disease | | 1 |
| | | 69 |

The 5 deceased workmen all died of causes unrelated to their occupation; cerebral haemorrhage, 3, motor accident, 1, and cardio-vascular disease, 1. In none of the cases was it possible to obtain a necropsy.

In 5 cases the radiographic appearances were considered to be compatible with sidero-silicosis but the clinical course of the condition together with the absence of adequate exposure to fibrogenic dust is held to discount the accuracy of this diagnosis. This opinion it is submitted is supported by the pathological findings in one case where lung tissue became available as a result of lobectomy undertaken for suspected malignant disease.

Detailed follow-up reports, illustrated by radiographs, are presented in 9 of the cases described in the original paper in 1950.

McLaughlin, and Harding [this *Bulletin*, 1957, v. 32, 157] criticized the original conclusions. Hamlin now states "no adequate reason has been demonstrated to alter the conclusion reached in our original study that the nodular patterns observed in these employees' chest roentgenograms represent mainly siderosis rather than silicosis". *A. Meiklejohn*

Pascal, Ingeborg & Werner, Inge. Über den Anteil von Cristobalit in Schamottemassen. [**The Formation of Cristobalite from Moulding Clay**] *Staub.* Düsseldorf. 1959, Feb. 1, v. 19, No. 2, 47–8, 2 figs.

Certain clays are major constituents of moulding sands in the production of steel castings. The action of heat may transform them partly into cristobalite and enhance the risk of silicosis among men fettling the castings. It is stated that animal experiments indicate that lung fibrosis is produced by cristobalite 3 times as rapidly as by quartz.

2 clays were heated in the range 900°–1,300°C. and the cristobalite contents were determined by X-ray spectrography. At 1,300°C. some 40% conversion to cristobalite resulted after an hour or two, but much less was found at lower temperatures. The yield depended very much upon the initial material. *C. N. Davies*

Sander, O. A. **Newer Concepts of the Pathogenesis of the Pneumoconiosis.** *J. Occupational Med.* Chicago. 1959, Jan., v. 1, No. 1, 7–11. [21 refs.]

Georgius Agricola in 1557 attributed disease of the lungs in metal miners to the "corrosive" action of the dust. This mechanical hypothesis of the pathogenesis of silicosis prevailed until about 1920, when it was supplanted by the silica solubility hypothesis. This in turn was criticized as inadequate [King *et al.*, this *Bulletin*, 1956, v. 31, 722–23]. Meanwhile there have been many other hypotheses. The current approach is that the fibrogenesis is due to an immunological process —antigen antibody reaction [Vigliani and Pernis, *ibid.*, 1959, v. 34, 347]. A major difficulty in all the hypotheses is to explain the reactions involved in the distinction between simple and complicated pneumoconiosis. In the latter tuberculous infection is considered to play an important if not the dominant part. At present no hypothesis of the pathogenesis of pneumoconiosis is wholly acceptable and so the discussions go on endlessly. The author—a clinician—poses the question: is there a dust which can be called truly inert when retained in the lungs, no matter how heavy the exposure has been? His summing up of the situation is that we should not engage in theoretical discourses but get back to the working places and rid them of highly injurious particles.

[There can be no dispute about the need for more intensive application of existing knowledge in the control of dust in mines and factories. This notwithstanding fundamental research involving theoretical discussions must proceed concurrently.] *A. Meiklejohn*

Magistretti, M., Sartorelli, E. & Tomasini, M. Studio dell'emodinamica polmonare in un silicotico pneumectomizzato. [**Study of Pulmonary Hemodynamics in a Pneumectomized Silicotic Subject**] *Med. d. Lavoro.* 1959, Feb., v. 50, No. 2, 114–19, 2 figs. [12 refs.]

The English summary appended to the paper is as follows:—

"Hemodynamic findings on the pulmonary circulation, in a patient with reticular-micronodular silicosis who underwent pneumectomy for an abscess in the left upper lobe, are reported as observed 4 years after surgical operation. Cardiac catheterization showed a hypertension in the pulmonary circulation, together with a marked increase of pulmonary arteriolar resistence, neither related to arterial hypoxemia nor modified by pure oxygen inhalation. The latter findings suggest an anatomic origin for the pulmonary hypertention (reduced capillary bed and reduced elasticity of arteriolar walls in the course of silicosis)."

SAWADA, Y. **[Roentgenological Studies on the Progress of Simple Silicosis (Roentgenological Studies on the Development of Silicosis: Report 1)]** *J. Sci. of Labour.* Tokyo. 1959, Mar., v. 35, No. 3, 203–28, 3 figs. [29 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"We have attempted to classify X-rays indicating the progress of silicosis in 7 grades, and the classification is called 'the typical course of silicosis'.

The classification is as follows.

Grade 1: Swelling of hilar lymph nodes and increase of lung markings are observed.
Grade 2: Scattered spotted densities begin to appear, and lung markings become linear.
Grade 3: Scattered appearance of nodular densities spreading all over the lung fields is observable.
Grade 4: Enlargement in size and increase in shadow of nodular densities are observable.
Grade 5: Confluence of nodular densities is observed.
Grade 6: Confluence densities are enlarged.
Grade 7: Massive shadows and emphysematous blebs are developed.

46 (64%) out of 72 silicosis patients observed in Sado Mine are 'the typical course of silicosis'."

MORROW, C. S. & STASKIEL, L. J. **Pneumoliths in Profusion in Silicosis.** *Amer. Rev. Tuberculosis.* 1959, Apr., v. 79, No. 4, 512–17, 4 figs.

"An unusual case has been reported demonstrating pneumoliths in profusion attributable to silicosis. This case has been termed unusual since such lesions are rarely seen in silicosis.

"The diagnosis in this case, made clinically, was based upon the following considerations: an adequate occupational history; exclusion of other disease in which similar densities may occur: and absence of other pulmonary evidence of silicosis on the roentgenogram."

FREOUR, P., LAUMONNIER, P., LÉGER, H., HIRSCH, O. & SALAUN, R. Sur un cas de silicose très tardivement reçonnu et diagnostiqué par biopsie pulmonaire. **[Case of Silicosis Recognized after Long Delay and finally diagnosed by Lung Biopsy]** *Arch. Malad. Professionnelles.* Paris. 1959, Mar.–Apr., v. 20, No. 2, 171–6.

The case is that of a workman aged 63 years, who had worked for the last 30 years as a builder's labourer. 3 years earlier he noted that he was short of breath on exertion. The breathlessness increased and his general health declined. Clinical examination revealed serious chronic bronchitis and emphysema. Radiographic examination of the lungs showed enlargement of the hila-diffuse fibrosis and discrete nodular opacities. A tuberculin test was negative. Treatment by cortisone and anti-tuberculosis drugs proved ineffective and the X-ray appearances remained unaltered. Resort was had to lung biopsy and this led to the diagnosis of silicosis. While employed as a builder's labourer the patient had been casually exposed to dust inhalation in the course of cement mixing. Investigation of the conditions of this work and the nature of the materials seemed to discount this as the cause. On more detailed exploration of the employment history it was discovered that earlier in his life the workman had worked for 3 months in a coal-mine and for 10 months in driving a tunnel. The authors emphasize that this type of case justifies provision in compensation schemes for such cases, where the disease is overlooked or does not develop for many years after exposure.

[Such cases are all too common and the most important fact which they underline is the need to record the patient's full employment history at the first consultation.] *A. Meiklejohn*

NOZAKI, S. & SAWADA, Y. **Progress of Simple Silicosis after the Patients quitting or changing their Jobs.** *Acta. Med. et Biologica.* Niigata. 1958, Dec., v. 6, No. 3, 181–7, 2 figs.

72 miners employed at a goldmine on an island in the Japan sea were submitted to X-ray examination of the lungs over periods of 3 to 15 years. The ore body was highly siliceous and cases of silicosis developed rapidly. After the diagnosis of silicosis some of the miners left the employment, while others continued in their occupation. As few of the patients left the island it was possible to follow their progress. For the purposes of recording their findings the authors devised a classification of the disease into 7 grades of increasing radiographic abnormality, of which the following are examples:

Grade 1: swelling of hilar lymph nodes and increase of lung markings.
Grade 3: scattered nodular densities all over the lung fields.
Grade 7: massive shadows with emphysematous blebs.

It was observed that the disease advanced irrespective of whether the workman continued in or left his occupation. The authors emphasize that the study included the war years when working conditions were extremely bad and not representative of ordinary conditions at this or other local mines. *A. Meiklejohn*

SATO, I., SATO, Y., MATSUOKA, M., INAGAKI, Y., KAJITA, A., TAKIZAWA, T. & HASEYAMA, H. **[Six Autopsy Cases of Primary Bronchial Carcinoma complicated with Pulmonary Silicosis]** *J. Sci. of Labour.* Tokyo. 1959, Mar., v. 35, No. 3, 229–40, 6 figs. [11 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"Autopsies of 18 cases of pulmonary silicosis were performed at Ikuno Mine Hospital (Hyogo Pref.) since 1955. Among these cases, 6 (33%) were accompanied with primary bronchial carcinoma. Otherwise, among 7 non-silicotic cases, which were autopsied there in the same period bronchial carcinoma was also detected in 3 cases. Silicotic cases complicated with bronchial carcinoma had some characteristics; most of these patients were of advanced age and all had only minimal or moderate silicotic changes. Freshly disseminated tuberculous foci were found in 2 cases. There were no specific features in the place of origin and in the histological classification (squamous cell carcinoma 3, adenocarcinoma 2 and oat-cell carcinoma 1) of cancer. While the occurrence of bronchial carcinoma is so evident as above mentioned, we can determine no cancerogenic environmental factor in Ikuno district."

JAHR, G. Silikose bei Bademeistern. [**Silicosis in Overseers of Baths**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1959, Jan.-Feb., v. 5, No. 1, 35-9, 1 fig.

The first reports on silicosis in overseers of sand baths were published in 1956 [see this *Bulletin*, 1957, v. 32, 459]. The author of the present paper critically re-examines the risks of exposure to silica dust of workers in institutions where sand baths are used in medical treatment. There is a description of the techniques of sand bath preparation in 2 hospitals and 2 sanatoria. Milled sand of particle size 3-4 mm. is transported to an elevated container where it is heated to 52-54°C. and then carried by a tube to movable wooden baths which are at a lower level. After use the sand is sterilized by heat, washed, dried, sieved and returned into circulation. The variations in procedure and the points at which fine silica dust entered the atmosphere in the 4 institutions are described. There is an account of a worker in 1 of these institutions where 40 sand baths a day were provided, who developed respiratory symptoms after about 16 years at the work. His physical state got worse and after another 7 years the diagnosis of silicosis was made. From this disease he died—26 years after the beginning of the employment.

The precautions that should be taken for the protection of sand bath workers are described at some length. These can be made most effective and there is certainly no need to prohibit sand bath treatment which, in the opinion of the author and others, is a valuable therapeutic medium. *M. E. Delafield*

THIEBLOT, L., CHAMPEIX, J., LAVARENNE, J. & TEULADE, R. Essai de traitement de la silicose par E.D.T.A. calcique. Note préliminaire. [**Treatment of Silicosis by Calcium E.D.T.A. Preliminary Communication**] *Arch. Malad. Professionnelles.* Paris. 1959, Mar.-Apr., v. 20, No. 2, 151-5.

In 1956 [this *Bulletin*, 1956, v. 31, 831] the occurrence of serious silicosis among workmen employed in the preparation of insulating material from diatomaceous earth was reported. The risk was greatest when the amorphous silica was calcined at high temperature, whereby cristobalite was formed. While the doctors recognized that prevention of the disease was the supreme need, they felt compelled to attempt some treatment of those already affected by the disease. The matter was urgent as cases of silicosis had occurred after 2-3 years' work in the processes, and, in fact, one case had been diagnosed after only 8 months.

13 patients were treated by a course of calcium EDTA. Preliminary investigation included clinical, radiographic, spirographic and haematological examinations, which were repeated periodically throughout the ensuing 12 months. The treatment involved the intravenous injection of calcium EDTA according to a scheme, details of which are set out in the article. Meanwhile the number of patients under treatment has been increased. The authors admit that no firm conclusions are possible for several years but feel that this preliminary notice of their project is justified particularly as 2 patients have already shown substantial clinical and radiographic improvement.

[The prevention of silicosis must always be the prime objective. Recent developments in specific therapy of the disease give hope that some, if not all patients, may in the near future benefit from drug treatment. Research in this field should be encouraged.] *A. Meiklejohn*

ANTWEILER, H. & HIRSCH, E. Weitere tierexperimentelle Untersuchungen zum Problem der Antikörperbildung bei der Silikose. [**Further Experiments on Animals to study the Problem of Antibody Formation in the Case of Silicosis**] *Ztschr. f. Immunitäts. u. Exper. Therap.* 1957, Aug., v. 114, No. 4, 378-92, 5 figs. [27 refs.]

In continuation of previous negative experiments with aerosil [this *Bulletin*, 1956, v. 31, 1232] the authors injected rabbits during 3 weeks repeatedly with ordinary quartz or with quartz which had previously been in contact with serum from the same animal and had then been freed from excess protein by repeated washing with Ringers solution. Antibody formation was assessed by observing under the microscope precipitation with the usual dilution technique, after mixing pretreated quartz with the serum of the injected animals. Positive results were obtained after 2 weeks, and in general the reaction was stronger when pretreated quartz had been injected.

Intravenous, intramuscular, intraperitoneal and subcutaneous injections all gave similar results, but after a single intrapulmonary injection the effect appeared somewhat later.

Similarly positive results were obtained with guineapigs. In another series guineapigs were injected with quartz, cristobalite, tridymite or vitreous silica and each antigen was tested against quartz as well as against the material used for injection. After 8 weeks the maximum strength of the reaction was reached and there was no evidence for specificity of the antibodies produced by the different forms of free silica.

Similar experiments with rats showed a considerably weaker power to produce antibodies, and there were considerable variations in strength of reaction for different animals.

The authors consider that quartz coated with protein is the antigen which produces homologous autoantibodies and state that they have started similar tests on silicotic miners. *G. Nagelschmidt*

Lupu, N. G. & Velikan, K. [**The Problem of Pneumoconiosis**] *Rev. Sci. Méd.* Bucharest. 1957, v. 2, 23–35. [11 refs.] [In Russian.]

The authors have carried out an experimental investigation of the pathogenesis of pneumoconiosis in which 1,000 guineapigs and rabbits were used. In guineapigs made to inhale air containing powdered silicon dioxide for 20 minutes each day thickening of the alveolar walls and mobilization of reticulo-endothelial cells were observed after 15 periods of inhalation. These changes were less marked in animals exposed to an aerosol of 2% novocaine solution before inhaling silicon dioxide. Animals similarly exposed to tobacco smoke showed infiltration of the alveolar walls and mobilization of the alveolar epithelium. The changes were abolished by preliminary inhalation of novocaine. Inhalation of smoke caused an increase in the total fat and calcium contents of the lungs. In animals subjected to vagotomy and novocaine blockade of the lung hila an increase in colloidopexis was observed in the alveolar epithelial cells; an increase was also produced by preliminary injection of acetylcholine or histamine. The effects of other substances and procedures are also described. *D. J. Bauer*

Giubileo, M. & Parmeggiani, L. Studio comparativo sulla determinazione della HbCO e del CO estraibile dal sangue. [**A Comparative Study on the Determination of HbCO and CO extractable from Blood**] *Med. d. Lavoro.* 1959, Feb., v. 50, No. 2, 91–107, 1 fig. [31 refs.]

The English summary appended to the paper is as follows:—

"Among the great deal of methods proposed for CO determination in the blood, the spectrophotometric and the gasometric methods are prominent. They underwent many modifications in over 50 years and they reached a high sensitivity and precision in the most refined procedures. Since a comparative study of the two methods was still lacking, it has been decided to perform it, in view of its interest for the pathogenesis. For this comparison the spectrophotometric methods of Heilmeyer ($HbO_2$–HbCO system) and of Kurz and Waller for the isobestic point (Hb–HbCO system), as well as the gasometric method of Scholander and Roughton (extraction with previous slight acidification with $CO_2$ in gaseous phase) were adopted. In order to establish the equivalence of the results, according to the formula: $HbCO\% = CO\ ml\%\ .\ 100/1{\cdot}343$ (total Hb g%–MetHb g%), the total Hb was determined by the cyanmethemoglobin spectrophotometric method of Michel and Stadie modified by Evelyn and Malloy; total blood iron was determined by the thiocyanate Wong's method modified by Grisler.

"First the magnitude of standard error was verified in the methods of Heilmeyer and of Scholander and Roughton. The degree of correlation between Michel and Harris's and Stadie's methods was determined and it was found very high ($r = 0{\cdot}99$). The interference of optically active substances present in plasma or blood on the spectrophotometric HbCO determination was studied and found to be considerable for bilirubin and for alimentary lipids during digestion (apparently 8 to 15% more HbCO in cases of alimentary lipemia and mild jaundice) and very high for methemoglobin if it is present in large amount in the blood.

"The comparison between the spectrophotometric and gasometric methods was performed on 10 cases of acute CO poisoning, 20 cases of chronic occupational exposure to illuminating gas, 11 cases of smoking habit, 20 cases of predisposition to the so-called endogenous oxycarbonemia (pneumocardiac diseases with and without pulmonary stasis, diabetes) and 7 control cases. The two methods showed a correlation $r > 0{\cdot}7$; in the acute poisoning group, the gasometric method gave higher values than the spectrophotometric method, while in all other groups the differences were neither significant nor univocal. Further investigations on guinea-pigs and human subjects showed that the excessive gasometric values observed in acute poisoning are neither due to the presence in the blood of subjects poisoned by illuminating gas of substances other than CO, capable of reducing Winkler's reagent, nor to the presence in the blood of a CO fraction bound to plasmatic substrata which could be extractable by means of Scholander and Roughton's method.

"A discussion follows on the advantages of the spectrophotometric method (quick, easy, its use can be suggested to laboratories which are already equipped with a spectrophotometer for other purposes) and on its disadvantages (requirement of a control of MetHb and other possible blood pigments; blood sample must be drawn from fasting patients; possible formation of hemachromogen compounds during treatment of the sample with strong alkali), as well as on the advantages of the gasometric method of Scholander and Roughton (minimum amount of blood, high sensitivity and precision, minimum expense and simple equipment) and its disadvantages (complicated handling, necessity of freshly made reagents: its use therefore is suggested for numerous routine analyses)."

Hasselt: Institut D'Hygiène Des Mines. Communication No. 159. Saturation oxyhémoglobinée et pression partielle de $CO_2$, au repos et à l'effort, dans la pneumoconiose des houilleurs [Brasseur, L., Tremouroux, J. & Kremer, R.]. [**Oxyhaemoglobin Saturation and Partial Pressure of $CO_2$ at Rest and after Exercise in Coalworkers' Pneumoconiosis**] 1959, Feb. 15, v. 14, No. 2, 21 mimeographed pp. + 12 pp. of tables, 4 figs. [30 refs.]

44 cases of coalworkers' pneumoconiosis were investigated at the Institute of Mining Hygiene at Hasselt, Belgium. In 6 patients of whom 2 suffered from simple pneumoconiosis and 4 from complicated pneumoconiosis, there was evidence of right heart insufficiency. The remaining 38 patients, whose ages ranged from 30 to 67 years, comprised 26 cases of simple and 12 cases of complicated pneumoconiosis. The special investigations included ECG examination, pulmonary ventilation at rest and after exercise—Fleisch bicycle ergometer—and measurement of blood *p*H and percentage oxygen saturation and $CO_2$ tension or blood obtained from the brachial artery.

The findings in each case are tabulated.

[In the 44 patients, the 45–49 age-group is the largest with 8 cases. These include 3 cases of simple pneumoconiosis and 5 cases of complicated pneumoconiosis. Other age-groups are similarly constituted. Such a small heterogeneous collection of cases does not justify any general conclusions.] *A. Meiklejohn*

DALLOZ, C., PERRIN, L. F. & RABAULT, J. Confrontation des résultats de l'exploration fonctionnelle pulmonaire avec le travail réellement effectué dans les mines par les ouvriers. **[Comparison of the Results of Pulmonary Ventilation Measurements with the Actual Performance of Miners at Work]** *Arch. Malad. Professionnelles.* Paris. 1959, Mar.–Apr., v. 20, No. 2, 137–47.

Physiological tests of ventilating capacity are increasingly relied upon in the assessment, for compensation purposes, of the impairment of capacity for work caused by pneumoconiosis. But the conditions under which the tests are carried out differ widely from those which exist on the actual job. Besides there may be psychological effects which follow the diagnosis of the disease and which variously influence the attitude to work of different individuals. Environmental conditions, too, vary widely between workplaces.

At the Institute of Industrial Medicine at Lyons 100 working miners (presumably coal-miners) suffering from silicosis were subjected to physiological tests of respiratory function. The tests included measurement of vital capacity and maximal voluntary ventilation per second at rest and after exercise on a bicycle ergometer. The results were assessed as a percentage of a theoretical normal value. The mine engineer recorded, according to a specially devised questionnary, the actual performance of each man at work.

Attention is particularly directed to the fact that healthy miners [possibly because of self selection for mining] frequently have ventilation levels substantially higher (105–120%) than the theoretical normal, so that values below normal represent not a slight but a substantial diminution and this is significant in relation to the heavy work of mining.

The estimates to be made by the engineer proved difficult. In some cases he confirmed the laboratory findings but in others he differed but this underlined the need for further investigations. *A. Meiklejohn*

SADLER, R. L. **Sputum-Positive Coalworker's Pneumoconiosis and Drug Therapy.** *Brit. J. Tuberculosis.* 1958, Apr., v. 52, No. 2, 163–6. [11 refs.]

Search of the tuberculosis registers at the Chest Clinic, Mexborough, Yorkshire, revealed that during the 8 years up to June 1956 27 mineworkers suffering from pneumoconiosis had received treatment for complicating tuberculosis. In all the cases tubercle bacilli had been found in the sputum on at least one occasion and all but 3 showed radiographic evidence of pulmonary cavitation. The cases were grouped according to radiographic appearances—PRU, Cardiff, classification. Group O comprised cases with category 1 simple pneumoconiosis together with unmodified reinfection type tuberculosis. Groups A, B and C were cases of progressive massive fibrosis [PMF] accompanied by active tuberculosis. All were observed for a mean period slightly less than 4 years after admission to the tuberculosis register. During this period the patients received combined drug therapy with streptomycin, isoniazid and PAS in various courses, for a minimum period of 9 months, excepting 5 patients in Group B and C who had no significant treatment. The 5 patients in Group O, that is those with unmodified pulmonary tuberculosis responded favourably, showing general and radiographic improvement and early sputum conversion, whereas the results of the sputum-positive PMF cases were quite unpromising.

In deciding on the line of treatment for sputum-positive PMF cases the following considerations are relevant: where the fibrosis is of greater degree than category A there is unlikely to be clinical improvement or sputum conversion with drug therapy; and persistence with this treatment may lead to chronic infectious cases becoming sources of drug-resistant tubercle bacilli. *A. Meiklejohn*

TAKÁCSY, L., BORDÁS, S. & TIMÁR, M. **Connective Tissue Changes caused in Guinea Pigs by Quartz, Quartz-Containing Dead Rock, Brown-Coal and Talc, as examined by the Method of Miller and Sayers.** *Acta Morphologica.* Budapest. 1959, v. 8, No. 4, 425–34, 8 figs. [12 refs.]

The English summary appended to the paper is as follows:—

"1. 104 adult guinea pigs of both sexes were tested for response to chemically pure quartz (Merck), to dead rock dust containing 77 per cent quartz obtained from a Hungarian coal mine, to quartz-free brown coal dust, and to talc, respectively. The method of testing was that described by MILLER and SAYERS.

"2. 1 to 3-micron fractions of the test dusts were injected intraperitoneally into guinea pigs under sterile conditions, giving single doses of 75 mg suspended in 2 ml of distilled water.

"3. The typical nodules developing in the abdominal peritoneum, alongside the linea alba, have been studied histologically 6 and 12 hours, as well as 1, 3, 5, 7, 10, 14, 20, 24, 30, 60 and 90 days following injection.

"4. The histological study of the nodules appears to be suitable for the demonstration of the fibrogenic properties peculiar to different dusts, if the various cellular and fibrous elements (mainly the macrophages, as well as the reticular fibres) are examined as inseparable parts of a unit, in the process of their development.

"5. The quartz-containing dead rock dust from the coal mine proved to be a fibrogenic agent similar to quartz. Talc proved to produce a fibrosis of 'storing' nature, different from that caused by quartz. The quartz-free brown coal dust elicited merely a 'foreign body' connective tissue response.

"6. The intraperitoneal test is recommended as a valuable procedure for the evaluation of the fibrogenic properties of industrial dusts."

GROSS, P., WESTRICK, Marian L. & McNERNEY, J. M. **Experimental Tuberculopneumoconiosis.** *Arch. Indust. Health.* Chicago. 1959, Mar., v. 19, No. 3, 320–34, 22 figs. [21 refs.]

At the Mellon Institute, Pittsburg, 4 groups, each of about 30 guineapigs, were dusted in an inhalation chamber for 6 hours daily, 5 days per week for one year. The dusts used were quartz (iron contaminated), aluminium oxide, silicon carbide and kaolin. 10 months after the first dust exposure one-half of the animals in each group were injected intratracheally with a standardized suspension of an avirulent human strain of tubercle bacilli. These animals were tuberculin tested and negative reactors were re-injected with a massive dose. An additional infection control group was treated with the suspension of tubercle bacilli only. After 2 injections no less than 44% of the infection control group remained tuberculin negative; an even higher higher incidence (56%) of negative reactors occurred in the silicon carbide group. During the first year, epidemics of pneumonia killed from 27% to 67% of the animals in the various groups and so some replacement animals were introduced.

After completion of the 12-month dust exposure the animals were pastured for a further 12 months. At various intervals animals died spontaneously and finally the survivors were killed at the end of the experiment.

Macroscopic Changes:

(a) Dust Controls: There were no remarkable pathological changes in the lungs of the uninfected guineapigs, including those exposed to iron-contaminated quartz dust. The absence of the expected silicotic changes, even at the end of the second year, was surprising.

(b) Tuberculous Infection Controls: In spite of the presence of 7 positive tuberculin reactors in this group, no gross lesion was found in the lungs or tracheal lymph nodes.

(c) Dusted-Infected Group: The lungs of some of the guineapigs which had been exposed to the various dusts and then infected with tubercle bacilli were similar to those of uninfected dusted animals. But the lungs of other dusted and infected guineapigs revealed significant differences. These consisted of foci of dense, unusually firm consolidation which varied from about 1 mm. in diameter to confluent areas occupying nearly an entire lobe. The lungs of guineapigs exposed to iron-contaminated quartz dust and subsequently infected with tubercle bacilli exhibited the highest incidence of the lesions and the severest involvement. In fact, these lesions frequently caused the death of the animal from inadequacy of functioning pulmonary parenchyma. In such lungs every lobe showed extensive consolidation. The lungs of guineapigs exposed to the other dusts and infected with tubercle bacilli were extensively involved by these peculiar consolidations in only a few instances, mostly one or several lobes were affected and then only focally.

The histological appearances of the lesions in the various groups are described in detail and illustrated by photomicrographs. The authors submit that the type of lesions produced by the combined action of a dust with a tuberculous infection is best identified by the generic designation of tuberculopneumoconiosis. The lesion is primarily a chronic proliferative alveolitis which results in obliteration of air spaces with fibrous replacement. It is emphasized that the potential of iron-contaminated quartz to produce tuberculopneumoconiosis is considerably greater than that of other dusts and silicon carbide is least able to produce this lesion.

Finally the question is raised whether any dust exists —even of the so-called "inert" type—which in conjunction with a tuberculous infection may not produce tuberculopneumoconiosis, provided that the concentrations of dust in the lung are sufficiently large and provided that the virulence of the infecting organism is adequate. *A. Meiklejohn*

SCHMIDT, K. G. & LÜCHTRATH, H. Die Wirkung von frischem und gebranntem Kaolin auf die Lunge und das Bauchfell von Ratten. **[The Effect of Raw and Calcined Kaolin on Lung and Peritoneum of Rats]** *Beiträge z. Silikose-Forschung.* 1958, No. 58, 1–37, 14 figs. [32 refs.]

In a lengthy introduction the crystal structure of kaolinite and the mineralogical changes which occur on heating are reviewed. This is followed by a survey of the literature on animal experiments with kaolin which leads to the conclusion that contradictory results were obtained by different workers, ranging from an inert to a fairly strongly fibrogenic activity for kaolin.

New experiments with intratracheal and intraperitoneal injections into rats of 50 mgm. of dust per animal are described. These were made (1) with raw kaolin; (2) with kaolin heated for one hour to 900°C., the product was mainly X-ray amorphous but contained small amounts of quartz and mica; (3) with kaolin heated to 1,200°C., the material contained much mullite and traces of quartz and cristobalite; (4) with a mixture of 30 mgm. quartz and 20 mgm. of raw kaolin. Previous results were available and used for comparison with (5) 50 mgm. of quartz.

The intratracheal injections were followed monthly up to 12 to 17 months after injection. No fibrotic reaction was seen with the raw kaolin; the 2 calcined samples reached King's fibrosis grade 1 after 3 to 4 months and did not progress further. The mixture of kaolin and quartz behaved similarly to pure quartz and gave fibrosis of grade 2 after 2 months and reached grade 5 after 9 months. All dusts reached the lymph glands, but the 3 kaolin samples did not cause fibrosis. Thus the raw kaolin was completely inert and the calcined kaolin gave only an extremely weak fibrogenic reaction.

The intraperitoneal tests were followed up to 7 or 8 months after injection. The raw and calcined kaolin produced nodules after 2 weeks which became collagenous after 3 weeks and reached a hyaline stage after 5 weeks, but the nodules continued to show the presence of dust cells. There was no further progression and very little difference between the 3 samples. The kaolin quartz mixtures and the quartz alone produced nodules faster than the kaolin and the concentric collagen structure was more distinct, but in the intraperitoneal test in rats kaolin was found to be strongly fibrogenic. The authors draw attention to this difference between lung and peritoneum, and warn against extrapolation of results from intraperitoneal tests in animals to those likely to occur in human lungs.

*G. Nagelschmidt*

Dünner, L. & Hardy, R. **Pneumoconiotic and Non-Pneumoconiotic Lung Lesions due to inhaling Dust and $SO_2$ Fumes from burning Coke. Clinical, Xray and Morbid-Anatomical Studies.** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 16, No. 6, 644–52, 7 figs.

In 1949 Dünner, Hardy and Bagnall [this *Bulletin*, 1950, v. 25, 481], of the Industrial Chest Diseases Clinic, Hull, England, reported their clinical and radiographic findings in 10 workmen, who had been employed at coke-fires involving exposure to coke dust and sulphur dioxide fumes. They claimed that pneumoconiosis resulted but in subsequent correspondence [*loc. cit.*] this was opposed by Fisher, the medical officer responsible for the supervision of the health of the employees at a large gasworks in London.

The subject of the present contribution is a series of 7 "coke-fire" men, who had been under clinical observation for several years and had died. In each case a post-mortem examination was performed and large sections prepared by Gough-Wentworth technique. The findings are presented in the following Table:—

[The evidence of this contribution and that of 1949 that exposure to the inhalation of dust and sulphur dioxide fumes at coke-fires causes pneumoconiosis is unconvincing. There is, however, a case for a scientific investigation of chronic respiratory disease among such workmen.]

*A. Meiklejohn*

Table. Summary of the radiological and morbid-anatomical findings

| Case No. | Age | Years of exposure | Chest X-ray | Morbid-anatomy | | | Other findings |
|---|---|---|---|---|---|---|---|
| | | | | Simple pneumoconiosis | Fibrosis (non-pneumoconiotic) | Bronchitis and emphysema | |
| 1 | 66 | 44 | Coarse reticulation | + | + | + | |
| 2 | 49 | 29 | – | + | + | + | Bronchiectasis, tuberculosis |
| 3 | 62 | 40 | – | + | – | + | |
| 4 | 67 | 6 | Diffuse fibrosis | – | +++ | – | |
| 5 | 62 | 48 | Marked striation | – | Patchy | + | |
| 6 | 72 | 52 | Coarse reticulation | + | – | – | Bronchial carcinoma |
| 7 | 50 | 29 | – | + | – | – | Bronchial carcinoma, tuberculosis |

Maranzana, P. Pneumoconiosi in lavoratori del cemento. Nota preventiva. [**Pneumoconiosis in Cement Workers. Preliminary note**] *Acta Med. Legalis et Socialis.* Liège. 1958, Oct.–Dec., v. 11, Nos. 3/4, 373–5.

The following is a translation of the author's summary:—

The author refers to the possibility of finding workers suffering from pulmonary silicosis among those engaged in the handling of finished cement. Of 69 cases discovered in cement workers at Casale, 9 were employed in successive stages of mining and 2 in bagging the finished product.

After discussing the difficulty of excluding possible contact with crude dusts during the long history of these workers, the author states that a series of clinical and mineralogical studies is not yet complete and that he intends soon to publish his conclusions on the subject.

*A. H. Phipps*

Champeix, J. & Moreau, H. L. Observations récentes sur les pneumoconioses par terre d'ocre. [**Recent Observations on Pneumoconiosis due to Ochre Earths**] *Arch. Malad. Professionnelles.* Paris. 1958, Nov.–Dec., v. 19, No. 6, 564–73, 5 figs.

15 workmen were employed at 3 separate plants for the treatment of ochre earths. These minerals were obtained from different geographical areas in France and owing to varying composition they were of different colour, yellow, red and black. The raw material was first ground by silica millstones, then sieved and bagged. The processes were carried out dry and were very dusty; many of the particles were under 3 microns.

For a few hours each year the workmen had to dress the millstones and this involved exposure—considered insignificant—to pure silica dust. All the ochre minerals contained silica, 5 to 35%, and iron, 62 to 73%.

4 workmen, aged 30 to 56 years, who had worked in the processes for 31, 22, 22½ and 8 years respectively, were found to have radiographic evidence of generalized micro-nodular pneumoconiosis. These cases were carefully studied over a period. The investigations comprised clinical and radiographic examination, comprehensive measurements of pulmonary ventilation at rest and after exercise, and oxymetry. It is admitted that some of the nodulation is probably silicotic but it is suggested that the fine diffuse reticular pattern represents siderosis. This is supported by the absence of symptoms, the non-progression of radiographic changes and the normal ventilation.

[The reproductions of radiographs are excellent and this contribution is commended to readers for the excellent presentation of the detailed findings in each case.] *A. Meiklejohn*

DÜNNER, L., HARDY, R., NAKIELNY, E., ROBINSON, L. B. & SMART, G. A. **Pneumoconiosis in Grain Workers, Oil and Flour Millers.** *Brit. J. Tuberculosis.* 1958, Oct., v. 52, No. 4, 291–8, 6 figs. on 2 pls. [14 refs.]

Flour and oil millers, silo and grain workers, and lightermen and bargemen, who handle cereal seeds and oil kernels, are exposed during their occupation to the inhalation of vegetable dusts contaminated in some instances by silica. 31 such workmen were investigated at the Industrial Chest Clinic, Hull, England. The salient findings in each of these cases, 5 fatal, are described briefly and illustrated by X-ray photographs in 4 cases. The data include age, nature and duration of occupation, clinical and radiographic changes, and pathological findings in the 5 fatal cases.

In 6 patients only were the radiographic appearances in the lungs considered to be normal. There were 10 cases of tuberculosis, 2 of bronchogenic carcinoma and several cases of pulmonary fibrosis. Simple pneumoconiosis was diagnosed histologically in 4 of the 5 fatal cases [this seems rather an exaggerated interpretation as judged by the case reports]. *A. Meiklejohn*

SCHILLING, R. S. F. **The Epidemiology of Byssinosis—Adventure and Misadventure.** *J. Occupational Med.* Chicago. 1959, Jan., v. 1, No. 1, 33–68, 1 fig. [26 refs.]

Occupational mortality rates for cotton workers published by the Registrar General in 1927 and 1938 suggested that the inhalation of textile dusts was a steady source of death from nephritis and a group of conditions in which the common factor was hyperpiesis. Examination of the mortality data indicated that much of the excess of cardio-vascular renal deaths in cotton workers was due to respiratory deaths and cor pulmonale. Schilling and his colleagues at the Nuffield Department of Occupational Health, Manchester, undertook a special enquiry into this problem [this *Bulletin*, 1952, v. 27, 936]. They concluded that hyperpiesis was not a serious occupational risk of cotton workers; the occupational mortality rates had misled them. But this misadventure was the beginning of a great adventure based on the coincidental observation that 66% of 131 card- and blow-room workers complained of tightness of the chest on Mondays, the characteristic symptom of byssinosis.

The rest of the article is a general recapitulation of the epidemiological studies in byssinosis already recorded in detail by Schilling in the Milroy Lectures [*ibid.*, 1956, v. 31, 1116–17]. *A. Meiklejohn*

HERRMANN, P. Staubmessungen am Arbeitsplatz. [**Dust Measurements in Workplaces**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1958, Sept.–Oct.–Nov.–Dec., v. 4, Nos. 5/6, 263–6.

A brief review of dust-sampling practice. A number of authors are cited but there are no references. *C. N. Davies*

HASSELT: INSTITUT D'HYGIÈNE DES MINES. Communication No. 158. Prélèvements de poussières sur une longue période dans un charbonnage témoin. 2e partie. Validité des mesures faites au "British Konimeter" dans les travaux préparatoires [DEGUELDRE, G. & CARTIGNY, S.]. [**Long-Period Dust Sampling in a Colliery. 2. Validity of British Konimeter Measurements in Preparatory Work**] 1959, Jan. 15, v. 14, No. 1, 54 mimeographed, pp. 15 figs.

After their consideration of the "P.R.U. Hand Pump" as a coal face dust sampler [this *Bulletin*, 1958, v. 33, 668] the authors continue with a critical assessment of the "British Konimeter" as a dust sampling instrument in preparatory work, where both coal and rock may be present. They show that with the standard technique of counting, the dust spot on the disk is often decentred, leading to discrepancies. If the disk is removed and replaced, *e.g.* for incineration, more than once, another error arises owing to loss of particles. Comparison of konimeters sampling simultaneously, with one thermal precipitator determination as a standard, showed that the results depended on the concentration and size analysis of dust clouds. Konimeter counts at 1,000 magnification, as used in the Institut d'Hygiène for thermal precipitator counts, indicated that particles cannot be seen properly at the standard 200 magnification, and so the cloud concentration affects the result because particles form pseudo-aggregates. Particles may be broken by impact with the disk, and others lost by blowing during sampling, the size of particles on the disk therefore differs from that of air-borne particles.

The conclusions are documented by numerous tables and graphs. The authors decided that konimeter counting must follow a strict system to get the best results. The approved technique fails to resolve particles of one micron and renders mistakes possible in judging between aggregates and particles. Consequently, they

have decided to abandon the konimeter for the sampling and control of the air in preparatory work.
*R. G. H. B. Boddy*

ROEBER, R. Messtechnische Erfassung von Feinstäuben. **[The Measurement of Fine Dust]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1958, Sept.–Oct.–Nov.–Dec., v. 4, Nos. 5/6, 254–63, 11 figs.

This is a descriptive account of the Zeiss konimeter, the Mines konimeter, the thermal precipitator, the Leitz tyndallometer, the Leitz tyndalloscope and a modification to the konimeter allowing continuous airflow in place of pump aspiration. *C. N. Davies*

FRIEDRICH, W. Die Feinheitsbestimmungen an technischen Stäuben. **[Determination of the Fineness of Technical Dusts]** *Staub.* Düsseldorf. 1959, May 1, v. 19, No. 5, 143–6, 4 figs.

The English summary appended to the paper is as follows:—

" The increasing importance of dusts in the technique of processes and the constant improvement of the measuring methods made it necessary to revise the " Directives for the Determination of the Fineness of Technical Dusts ", in existence since 1936. The first part of the article describes the necessary preparations for the determination of fineness, such as, for example, the taking of samples, and also describes the methods of examination. The second part treats the evaluation and the graphic representation of the values found by the measuring technique."

ROEBER, R. Photometrische Auswertung von Feinstaub-Präparaten. **[Photometric Evaluation of Deposits of Fine Dust]** *Staub.* Düsseldorf. 1959, Mar. 1, v. 19, No. 3, 73–8, 7 figs.

This paper discusses in a general way the use of photocells for measuring dust samples taken with a konimeter. The fundamental difficulties of the method, due to rapid changes of optical screening with particle size, the influence of refractive index and of optical transmission, and the difficulty that the larger particles have an overwhelming effect, are hardly touched upon. Without considerable attention to these problems the methods described would be of value only in controlling dust of quite definite characteristics. *C. N. Davies*

RAMMLER, E. & BAUERFEIND, R. Staubmessungen in Braunkohlenbrikettfabriken. **[Dust Measurement in Lignite Briquette Plants]** *Staub.* Düsseldorf. 1959, May 1, v. 19, No. 5, 134–9, 5 figs. [10 refs.]

The English summary appended to the paper is as follows:—

" The first part of the article refers to the dust quantities accumulating in lignite briquette plants, the places where they accrue there and the possibilities of removing them. Then there follow detailed observations on the peculiarities in the technique of measuring for the determination of the degree of dust precipitation in brown coal briquette works, which are examined, according to type of precipitation, by means of a series of measuring instances."

DAWES, J. G. & MAGUIRE, B. A. **Calculation of the Relationships between Particle Number, Area and Weight Concentration in Coal-Mine Dust Clouds.** *Safety in Mines Research Establishment* [Portobello St., Sheffield]. *Research Rept.* No. 150, 1958, Dec., 26 mimeographed pp., 16 figs. [11 refs.] [2s. 9d.].

" From information available on the size-distributions of coal-dust clouds in coal mines, the variations in the conversion factors relating particle number to surface area and to weight measurements of dust concentration have been computed. The variations are not much reduced by the use of a size-selector designed to eliminate non-respirable dust particles. The weight to area conversion factor, when using a size-selector, is shown to have the smallest variation of those examined."

IVERS, E. J. Internationaler Stand der Prüfsiebung. **[International Position of Test Sieving]** *Staub.* Düsseldorf. 1959, May, 1, v. 19, No. 5, 146–9, 3 figs.

HASENCLEVER, D. Über die Prüfung von Filtern zur Abscheidung radioaktiver Aerosole. **[Testing Filters for Use with Radio-active Aerosols]** *Staub.* Düsseldorf. 1959, Feb. 1, v. 19, No. 2, 37–43, 13 figs. [14 refs.]

3 methods are described. The first employs a cloud of quartz dust containing 15,000 to 20,000 particles per cc. of which 80% are below 2 micron diameter, 16% from 2 to 5 and the rest over 5. A Leitz tyndallometer, with a 30-watt lamp to increase its sensitivity, was used to compare the dust concentrations upstream and downstream of the filter.

The second system made use of a fine spray of paraffin oil. The author rejects American practice of using a cloud of uniformly-sized droplets of di-octyl phthalate, produced by condensation, on the grounds that a misleading idea of filter efficiency could result if the particle size of the homogeneous aerosol differed from that for which the filter efficiency was minimal. The reader, however, should remember that the size of the di-octyl phthalate particles can be adjusted and set to that giving maximum penetration.

Particle size was determined as a weight mean by allowing the droplets to settle upon a flake of mica, weighing and counting under dark ground illumination. This gave 1·1 ± 0·4 microns, the uncertainty being due to the difficulty of weighing a few $\gamma$ on a 370 mgm. slip of mica. Since the deposition times were 40 to 95 hours the cloud must have changed by coagulation and isothermal distillation so that the above size is certainly too great. The mean apparent diameter of droplets on a thermal precipitator slide was 0·6 to 0·8 microns hence, allowing for spreading, it is probable that the original droplets were mainly between 0·3 and 0·6 micron with a maximum of 1·0.

The final test used a radio-active aerosol of particles below 0·3 micron. Dry air, free from particles exceeding 1 micron, had thoron added to it which deposited radio-active atoms of thorium B on the fine atmospheric particles. The cloud was passed through up to 9 filters in succession and the deposition in them measured by their gain in radio-activity. An exponential decline in the activity on successive filters was observed, hence, with the non-uniform cloud, any size-selection by the earlier filters must have been obliterated in some way.

Only a few particles could be seen on thermal precipitator samples, with dark ground illumination, but autoradiographs revealed heavy deposits. It is considered that no particles exceeded 0·6 micron while most were below 0·3.

All the filters tested were found to be less effective against the radio-active aerosol than they were for quartz dust. The nature of the test aerosol had more influence on filter performance than changes in fibre diameter or air flow.

A comparison of the oil mist with the radio-active cloud showed fair agreement as long as the filter contained few fibres coarser than 1 micron diameter.

A rate of air flow giving minimal deposition was observed for a paper filter used against quartz dust. Since the dust concentration in these experiments was constant the rate at which dust entered the filter increased with the air flow and it is concluded that the efficiency of filtration is related to the amount of dust in it for which a critical value exists giving minimum deposition at about 20 gm./m².

With oil mist, or the radio-active aerosol, a rise in air flow caused an increase in the efficiency of paper filters which reached a limiting value (90–100%) for velocities over 3 m./sec. This agrees with the results of BLASEWITZ and JUDSON (*Chem. Engineering Progress*, 1955, v. 51, 6, 0·2–0·7 micron) and HUMPHREY and GADEN (*Indust. & Engineering Chem.*, 1955, v. 47, 924, Ca. 1 micron). *C. N. Davies*

WALKENHORST, W. Aerosolfiltration mit Membranfiltern im Teilchengrössenbereich unterhalb 0,1 Mikron. **[The Performance of Membrane Filters against Aerosols Containing Particles Smaller than 0·1 Micron]** *Staub.* Düsseldorf. 1959, Mar. 1, v. 19, No. 3, 69–72, 6 figs. [10 refs.]

The aerosol consisted of particles of tungsten oxide formed by evaporation from a red hot tungsten wire in air. The cloud was sampled up and downstream of the filter by a pair of thermal precipitators provided with platinum deposition slips coated with a thin, detachable film of collodion. The film, carrying the aerosol deposit, was stripped off for examination by electron microscopy.

The size-distribution curves and number concentrations were determined for each sample and by comparing them at corresponding sizes curves of filter efficiency against particle size could be deduced.

A general tendency was observed for filtration efficiency to decrease with particle size down to the limit of the experiment at 0·005 micron. No size was observed at which filtration was minimal.

*C. N. Davies*

ZEHR, J. Die experimentelle Bestimmung der oberen Zündgrenze von Staub/Luft-Gemischen als Beitrag zur Beurteilung der Staubexplosionsgefahren. **[Experimental Measurement of the Upper Ignition Limit of Dust-Air Mixtures in Relation to the Evaluation of Dust Explosion Dangers]** *Staub.* Düsseldorf. 1959, May 1, v. 19, No. 5, 204–14, 3 figs. [40 refs.]

The English summary appended to the paper is as follows:—

"After pointing to the significance of the upper ignition limit for dust explosions, there follows a description of an apparatus, with which series tests with many combustible dusts can be executed, together with details of the evaluation method appertaining thereto. A number of results are quoted and the potentialities of application are discussed on the basis of these results. The closing part treats safety measures with special pointers for several cases in practice."

MÖSSMER, G. Über eine neue Absaugehaube für Steinmetzarbeiter. **[A New Exhauster Hood for Stone Cutters]** *Staub.* Düsseldorf. 1959, Apr. 1, v. 19, No. 4, 102–3, 6 figs.

The English summary appended to the paper is as follows:—

"The article gives a report on a new exhauster hood for stone cutters, which is distinguished by a particularly good suction range. This apparatus, which can be put to manifold uses and is easy to handle, has been tried out in customary performance and has stood the test absolutely. Dust measurements showed that the exhauster hood fulfils the requirements demanded."

BARTH, W. Grundlegende Untersuchungen über die Reinigunsleistung von Wassertropfen. **[Fundamental Investigations on the Cleaning Capacity of Water Drops]** *Staub.* Düsseldorf. 1959, May 1, v. 19, No. 5, 175–80, 12 figs. [12 refs.]

The English summary appended to the paper is as follows:—

"The possibility to remove dusts from gases by wet cleaning is of great practical importance for many branches of industry. The work presented herewith reports on fundamental investigations into the cleaning capacity of water drops. The values determined with the aid of the described computing method are compared with measurings and a number of practical conclusions are drawn in relation to the development of wet cleaning plants."

LEAD INDUSTRIES ASS. **The Lead Hygiene Conference. November 6–7, 1958, Chicago, Illinois.** *Indust. Med. & Surgery.* Miami. 1959, Mar., v. 28, No. 3, 93–163, 19 figs. [Numerous refs.]

Work that is new and views that are familiar emerge from these 12 papers and discussions, reported apparently in full. Though clinical lead poisoning may be rare the potential threat is a reality. At the last conference 10 years ago emphasis was given to the need for the partnership of engineering and medical skills, and now new research has much to offer the team. Methods of analysis of lead in blood and urine are improving. The U.S. Public Health Service has co-ordinated a scheme for evaluating blood analyses. There is still no way of studying the amount of lead fixed in the skeleton.

Clinical examinations, serial tests for stippled cells and haemoglobin and occasional urine porphyrin tests proved effective in estimating levels of lead absorption over a period of 28 years: this is the conclusion of the E. L. BELKNAPS in their paper *Clinical Control of Health in the Storage Battery Industry* (pp. 94–101), in which they compare qualitative with quantitative tests.

It was hoped that one point of controversy could be ended by H. B. ELKINS' study since 1950 of *The Lead Content of Water from Red-Lead Painted Tanks* (pp. 112–16). 70 samples of water were analysed from 11 standpipes; only 3 samples contained significant amounts, and these were from tanks in standby service. Further panel tests indicated that no significant quantity of lead would be added by the paint if the daily consumption approached the tank capacity.

A review of the literature and theories concerning the high summer incidence of acute episodes is given in *Effects of Season and Temperature on Childhood Plumbism* (pp. 137–43) by A. M. BAETJER who describes experiments to test the effects of environmental temperature and humidity on the susceptibility of mice to lead poisoning. Heat, especially if continuous, enhanced both acute and chronic effects.

H. D. SMITH in *Lead Poisoning in Children and its Therapy with EDTA* (pp. 148–55) also shows that saturnism in children caused by pica from crumbling paint, is a socio-economic problem. Encephalopathy occurs in one-third of all childhood lead poisoning; the threat is to brain and life. To remove as much lead from the soft tissues as possible, EDTA is used, though far from ideal. Cerebral symptoms were exacerbated in the first day or 2 of treatment, and now it is given gradually, testing with 25 mgm./kgm. of body weight for 1 day and continuing with 75 mgm./kgm. daily for 4 days. Attempts to decrease cerebral metabolism by hypothermia so far have had little success, though further trials are advocated.

L. H. MILLER in *EDTA Therapy in Persons with Excessive Lead Absorption from Industrial Exposure* (pp. 144–7), after describing the pharmacology of chelating compounds, concludes that EDTA is useful in the acute stage, shortening disability or unemployment; sometimes it fails. Of value in children, it should be used with caution in adults who will recover in any case if removed from exposure. It has no place in prophylaxis and may cause blood and urine analyses to be misleading for diagnostic and medicolegal purposes.

*Responses of Human Subjects to Lead Compounds* (pp. 156–61) is R. A. KEHOE'S progress report of his investigation with atmospheric finely divided lead sesquioxide. With respiratory exposure for 5 days each week instead of 7 the rate of urinary excretion and the concentration in the blood reaches a plateau. If lead is given by the mouth every day the concentration in the blood and the accumulation in the body goes up at a steady rate for as long as 5 years. When a change is made in the size of the particles, small particles, 0·5 micron, are retained in the lung to the extent of 35–40% and the larger ones, 1 micron, 40–50%. Many 3-micron particles are strained out in the upper respiratory tract and swallowed, sharply increasing the faecal content, and the total rate of lead absorption, in proportion to the lead content in the air, decreases.

Other papers on health control, hygienic standards, precautionary labelling, errors in diagnosis and legal considerations and also the well argued discussions brought to light many aspects of lead poisoning, for example the mistake of establishing plumbism on purely laboratory tests. The conference points the lesson: the subject of plumbism is a sick person.

*M. Patricia Fitzsimons*

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HADENGUE, A. & LAMBERTON, J. N. Saturnisme ou présaturnisme accidentels. **[Accidental Lead Poisoning]** *Arch. Malad. Professionnelles.* Paris. 1959, Jan.–Feb., v. 20, No. 1, 87–9.

The variations in the proportion of stippled red cells observed in the blood of individual workers in lead from time to time at routine examinations have led some experts to doubt the value of the stippled cell count for an assessment of the extent of lead absorption. The author does not share this opinion and gives 3 examples in support of his own view. The cases described were in 3 workers at an accumulator factory. In all these workers a sudden rise in the numbers of stippled cells led to special enquiry and the discovery of accident at work. The first case occurred in a young worker whose stippled cell count on 7 occasions during the 5 months after engagement had never been above 20 per 100 white cells. A few days after the last of these examinations the count, made at another laboratory because the worker had stayed away from work with a digestive disturbance, had risen to 110 per 100. On return to work about 14 days later the count was 127 per 100. This raised the suspicion that he had in some way absorbed an unusual amount of lead. It was found that within 2 or 3 days after the last low count a container holding 225 kgm. of powdered litharge had broken and distributed the powder close to the worker who was filling a mixer with the chemical.

The other 2 cases were of similar character in that a sudden rise in the basophilic cell count led to enquiry and the discovery of an accident at work.

*M. E. Delafield*

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WALDMAN, R. K. & BORMAN, E. K. **A Note on Serum Transaminase Activity after Lead Absorption.** *Arch. Indust. Health.* Chicago. 1959, Apr., v. 19, No. 4, 431–3. [16 refs.]

" In a study of persons exposed to lead it has been shown that SGO-T activity was increased when blood lead concentrations were elevated, in this instance without clinical symptoms of poisoning. This observation, coupled with results obtained by others on animals exposed to carbon tetrachloride, suggests wider use of the determination of serum transaminase activity to study correlation of results with exposures to these and other substances which cause cell damage, particularly in the liver.

"The study of serum transaminases may prove a useful means for reassessing currently accepted threshold limits and a practical guide for industrial physicians in the control of industrial exposures."

Verbanck, M., Toussaint, C., Toppet, N., Bastenier, H., Deslypère, P. & Degraef-Millet. Étude métabolique des effets de l'E.D.T.A. calcique dans le saturnisme latent. [**A Study of the Metabolic Effects of CaEDTA in Latent Lead Poisoning**] *Arch. Malad. Professionnelles.* Paris. 1959, Jan.–Feb., v. 20, No. 1, 21–33, 2 graphs. [32 refs.]

The purpose of the investigations described in this paper was to study the effect of CaEDTA administration to men with latent lead poisoning on the urinary excretion of lead and of certain mineral substances. A clinical account is given of the 6 men on whom the study was made. CaEDTA was given to some of the men in a daily intramuscular dose of 1·2 gm. and to the others in an intravenous dose of 2·4 gm. The analyses conducted on both blood and urine were (1) creatinine—to assess the urinary glomerular function, (2) calcium, (3) phosphorus, (4) lead, (5) magnesium and (6) potassium. The findings are described with a number of tables of statistical data.

The number of men on whom the investigations were made was small but among the conclusions it is stated that in latent plumbism EDTA (1) does not bring about the mobilization of an appreciable amount of the lead stored in the bones, (2) depresses the activity of the parathyroids and hence the liberation of calcium and of lead from the bones is curbed, and (3) diminishes the excretion of monovalent ions, notably potassium.

*M. E. Delafield*

Quino, E. A. **Field Method for the Determination of Inorganic Lead Fumes in Air.** *Amer. Indust. Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 134–7, 1 fig.

Fried, Joan F., Lindenbaum, A. & Schubert, J. **Comparison of 3 Chelating Agents in Treatment of Experimental Manganese Poisoning.** *Proc. Soc. Exper. Biol. & Med.* 1959, Mar., v. 100, No. 3, 570–73. [13 refs.]

In 30-day survival studies on rats poisoned by an LD90 of Mn gluconate, diethylenetriaminepentaacetic acid (DTPA) and EDTA gave significant protection, DTPA more so as was to be expected from a calculation of the relative effectiveness of the chelating agents, whereas EBAA [ethylene bis(*a*-imino-O-hydroxyphenylacetic acid)] did not. (Separate toxicity tests showed that intravenously 70 mgm./kgm. of EBAA for 3 days and 250 mgm./kgm. of CaDTPA, were apparently harmless and that intraperitoneally 1490 mgm./kgm. of CaEDTA and 1830 mgm./kgm. of CaDTPA, just less than the equimolar level (2000), resulted in 100% survival.)

Mn gluconate in a 3·5% solution, at 27 mgm./kgm. as Mn, intraperitoneally, was followed by intravenous injections of CaDTPA or CaEDTA (ethylenediaminetetraacetic acid) in equimolar ratios, doses being expressed as the acid forms, or of EBAA as the tetrasodium salt. 158 mgm./kgm. of CaDTPA or 118 mgm./kgm. of CaEDTA resulted in complete protection when given 3½ hours, and in 50% survival when given 5 hours after poisoning the average survival time being longer with CaDTPA. Mn chelates of DTPA and EDTA intraperitoneally in doses of 130, 162·5, 195 or 225 mgm./kgm. Mn gave survival rates of 100, 100, 100 and 94% with MnDTPA and of 100, 83, 70 and 60% with MnEDTA.

Tissue distribution studies were made on rats injected intravenously with $^{54}MnCl_2$, 1 $\mu$c per rat, and, 1 hour later and on the following 2 days, with EBAA at 80, 40 and 40 mgm./kgm., or CaEDTA in equimolar ratios to this (65 and 32·5 mgm./kgm.), or CaEDTA at 200 mgm./kgm. per injection, or saline, and killed the next day. The EBAA group showed no significant differences compared with the saline controls; the Mn excretion pattern was also unaltered. The equimolar dose of CaEDTA produced a small, significant shift from faeces to urine; the larger dose increased this and also lowered the Mn content of the kidneys by 20%.

[See also this *Bulletin*, 1956, v. 31, 546.]

*M. Patricia Fitzsimons*

Hardy, Harriet L. & Tepper, L. B. **Beryllium Disease. A Review of Current Knowledge.** *J. Occupational Med.* Chicago. 1959, Apr., v. 1, No. 4, 219–24. [18 refs.]

Cash, R., Shapiro, R. I., Levy, S. H. & Hopkins, S. M. **Chelating Agents in the Therapy of Beryllium Poisoning.** *New England J. of Med.* 1959, Apr. 2, v. 260, No. 14, 683–6, 3 figs. [16 refs.]

This is the report of a pilot study. 2 patients with chronic beryllium disease were given the chelating agent EDTA for 3 and 4 days and the effect on the excretion of beryllium in the urine was measured. An increase in the beryllium excretion during the trial period compared with the control period is shown. The nature of chelation, its theoretical application and its therapeutic implications in the treatment of beryllium disease are discussed.

[Inadequate details of the method of the experiment are given. The technique for estimating the microgramme quantities of beryllium involved was spectrographic but no limits of error, which may be considerable, are given. The period for establishing the "control" level of beryllium in the urine before the administration of EDTA was 2 days in one case and unstated in the other. In view of the considerable variation in daily excretion and the difficulties of accurate estimation of beryllium, the results of this pilot study need confirmation before discussion.]

*C. H. Wood*

Smith, R. G., MacEwen, J. D. & Barrow, R. E. **Sampling and Analysis of Phenols in Air.** *Amer. Indust. Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 142–8, 5 figs. [11 refs.]

Campbell, E. E., Milligan, M. F. & Miller, H. M. **Evaluation of Methods for the Determination of Halogenated Hydrocarbons in Air.** *Amer. Indust. Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 138–41.

Truhaut, R., Paoletti, C., Boiron, M. & Tubiana, M. Études expérimentales sur la toxicologie du benzène. Modifications de l'érythropoïèse suivies par le fer radioactif. [**Experimental Studies on the Toxicology of Benzene. Modifications of Erythropoiesis followed by the Use of Radioactive Iron**] *Arch. Malad. Professionnelles.* Paris. 1959, Mar.–Apr., v. 20, No. 2, 121–36, 5 figs. [35 refs.]

In these elaborate experiments, 10 rabbits were injected subcutaneously each day with 1 ml. of an 80% by volume solution of benzene in oil, and another 10 were exposed to an atmosphere concentration of 6 mgm./litre of benzene for 8 hours a day on 6 days a week, until there was almost complete anorexia and great loss of weight. In the first group this took 4–19 days, and in the other 30–125 days. At selected times after the onset of poisoning $^{59}$Fe (1 millicurie per mgm.) was injected intravenously after fixation on autologous or homologous rabbit plasma, and its disposal was determined by the rate at which it disappeared from the plasma and appeared in the red blood cells. Autologous plasma from the experimental animals was manipulated in this way: 10 ml. blood or 5 ml. plasma was mixed with $^{59}$Fe solution, kept in a water bath for ½ hour and reinjected intravenously, 4–7 microcuries being given. Homologous plasma from the 22 control rabbits was manipulated in this way: a control animal, which had received its autologous plasma with 20–25 microcuries 40 minutes previously, was killed by cardiac puncture from which 50–100 ml. blood were withdrawn and centrifuged; after its radioactivity was measured, this plasma was injected into the experimental animals, from which 15 ml. blood were first removed. By this means, the benzene poisoning should not interfere with the plasma iron fixing proteins.

Serial samples of blood were withdrawn, frequently for 12 hours and centrifuged, then daily and weekly, and the radio-activity was measured. Coefficients expressing plasma disappearance of the radio-active iron in the control and the poisoned animals and coefficients of the maximum utilization of the radio-active iron by the red cells are reproduced in tables. By whichever route poisoned and whether for long or short periods, there were some animals with a hyperplastic response of the blood forming tissues, shown by acceleration of iron metabolism in the plasma and the red cells, and others with the reverse effects. In some others there was a qualitative modification of erythropoiesis, a dissociation between disappearance from plasma and appearance in red cells. *M. Patricia Fitzsimons*

Friebel, H. & Stein, A. Zur Genese des durch einfache Chemikalien hervorgerufenen Asthmas. Versuche mit p-Phenylendiamin. [**Asthma Induced by Simple Chemicals: Experiments with p-Phenylenediamine**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 16, No. 6, 620–29. [22 refs.]

The asthmatic condition found in fur dyers first described in 1920 was considered at that time to be an anaphylactic state brought about by exposure to p-phenylenediamine which was used as a dye. This asthma was called " Ursol " asthma. Medical opinion has been divided on the question of whether " Ursol " asthma is the result of allergy or is caused by the chronic inflammatory changes in the respiratory system brought about by p-phenylenediamine. The experiments here described were designed to test this question of causation. Several groups of guineapigs were given subcutaneous injections of the distilled chemical or of the hydrochloride or the oxidized form. At a later date the animals were made to inhale aerosols of watery solutions of the chemical substances. The results of the experiments are fully described with tables. In 1,091 inhalation experiments 55 animals had asthmatic disturbances of breathing which set in after 3–12 minutes from the beginning of the inhalation. These attacks of dyspnoea occurred not only in the animals prepared by the chemical injections but also in control animals. The conclusion drawn from this work is that the attacks of dyspnoea " are mainly caused by toxic irritation of the respiratory system. The possibility of allergic-anaphylactic mechanism involved in 'Ursol'-asthma could not be excluded, but we found no evidence to support this hypothesis." *M. E. Delafield*

Henson, E. V. **Toxicology of some of the Aliphatic and Alicyclic Hydrocarbons.** *J. Occupational Med.* Chicago. 1959, Feb., v. 1, No. 2, 105–12. [29 refs.]

This is a brief review of the chemistry of the 4 homologous series of aliphatic hydrocarbons. Many compounds with similar molecular configuration have similar toxic effects, but generally only when their actions are physical and not chemical. By learning some chemistry we may learn some toxicology, and this becomes necessary because of new or vaguely described harmful chemicals that people meet in industry and in their everyday lives. Attempts have been made to correlate some physical property such as boiling point or solubility to toxic effects, and in many homologous series each succeeding member is more toxic than the preceding one. The difficulty is that when toxic effects occur from chemical action the predicted intoxicating dose can be wrong. Information is needed concerning human exposure. Aliphatic hydrocarbons have solvent, narcotic and irritant properties and are not thought to have any significant harmful effect on the haemopoietic system; myocardial sensitization occurs with some.

Saturated hydrocarbons, paraffins or alkanes ($C_nH_{2n+2}$) are characteristically inert, practically insoluble in water but soluble in most organic liquids. They occur in natural gas, petroleum and vegetable oils. Methane and ethane are physiologically inert. The higher members may be considered as mixtures; gasoline and kerosene are complex mixtures of $C_5$–$C_9$ hydrocarbons and often contain indefinite amounts of aromatic compounds of the benzene (benzol) type and of 5- and 6-carbon saturated and unsaturated cyclic compounds. Some intoxication symptoms caused by the benzene have been attributed to the paraffin group, but any suppressing effect of the aliphatic hydrocarbons on blood formation is slight. The term benzine is archaic and misleading and should not be used alone; petroleum benzine (benzin) should only be used for material meeting the U.S. Pharmacopoeia XIV specifications; the term ligroin should be used instead of benzine or petroleum ether.

Ethylenic hydrocarbons, alkenes or "olefins" ($C_nH_{2n}$) are unsaturated, characterized by a double bond and therefore highly reactive and so do not occur in natural products. They differ little from the alkanes in physical properties but contrast sharply with them in chemical properties. Acetylenic hydrocarbons or alkynes ($C_nH_{2n-2}$) have a triple bond, this higher degree of unsaturation being associated with still greater chemical reactivity.

Alicyclic hydrocarbons or polymethylene compounds are cyclic and have aliphatic properties. Cyclopropane, the first of the series, is an isomer of prophylene $C_3H_6$. Unsaturation can exist in the ring, double unsaturation beginning with the 5-carbon member, cyclopentadiene. Complex polycyclic compounds occur naturally in petroleum, terpenes, camphors and in the cholane nucleus in bile acids, sterols and digitalis.

*M. Patricia Fitzsimons*

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FINULLI, M. & GHISLANDI, E. La frequenza del diabete nella intossicazione cronica da solfuro di carbonio. [**Incidence of Diabetes on Chronic Carbon Disulphide Poisoning**] *Med. d. Lavoro.* 1959, Mar., v. 50, No. 3, 189–92. [15 refs.]

The English summary appended to the paper is as follows:—

"In a group of 102 patients with vascular diseases due to chronic exposure to $CS_2$ vapours, hospitalised in the Clinic for Occupational Diseases of the University of Milan in the last 14 years, 6 cases of senile diabetes were observed. In two other cases diabetes appeared after a diagnosis of carbon disulphide encephalovasculopathy had been established; all cases were insulin-sensitive; none had a familiar history of diabetes. By comparison with the incidence of diabetes in the general population, as indicated from various sources and with the incidence observed in a personal investigation on 1500 male subjects comparable by age and social status to the 102 patients, the incidence of diabetes appears definitely high in patients with chronic $CS_2$ poisoning. Since it is known that chronic $CS_2$ poisoning induces vascular lesions mainly in the brain and kidneys, it is suggested that such vascular lesions may involve other organs including the pancreas and thereby be responsible for the described changes in glucides metabolism."

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MICHALOVÁ, C., BARTONÍCEK, V. & ZÁSTAVA, V. Organotoxische Wirkungen von Schwefelkohlenstoff nach parenteraler Intoxikation von Kaninchen. [**The Toxic Action of Carbon Disulphide on the Tissues**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 16, No. 6, 653–65, 8 figs. [Numerous refs.]

In this study of the toxic action of carbon disulphide, 10 rabbits were given intramuscular injections of 0·1 ml. of the pure substance in 0·2 ml. of sterile olive oil 3 times a week over a period of months. There were 5 control animals. A number of biochemical analyses of urine and blood were carried out weekly. Weight and blood pressure were recorded. Many histological examinations of the animal tissues were carried out and the results of these are fully described with 8 photomicrographs. The study was originally planned to last 12 months but by the end of the 7th month 7 of the experimental animals had died and 2 were killed because of extreme cachexia.

The main finding in the biochemical tests was a very marked increase in blood cholesterol. The changes observed in the histological study are fully described and of these the most prominent was a general disturbance of capillary permeability which was most marked in the liver and the kidneys.

*M. E. Delafield*

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BRITISH MED. J. 1958, Dec. 6, 1408–9. **Carbon-Monoxide Poisoning. Use of Carbon-Dioxide-Oxygen Mixture.** Statement by the MEDICAL RESEARCH COUNCIL.

In February 1955 the Medical Research Council recommended that ambulances should no longer carry carbogen ($O_2$ containing 5–7% $CO_2$) for the first-aid treatment of patients in respiratory failure (*Brit. Med. J.*, 1955, v. 1, 313).

A special sub-committee of the Council has now reviewed recent evidence from animal and human experiments and the Council have decided that 5% carbogen is, as previously believed, the best treatment for carbon-monoxide poisoning. The carbogen, by stimulating the respiratory centre secures more rapid replacement of CO than pure oxygen. The decision as to which gas to use in first-aid treatment is left to first-aid personnel who can usually decide whether CO-poisoning or other types of asphyxia are responsible.

*M. L. Thomson*

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SAITA, G. I fattori del complesso protrombinico nelle intossicazioni acute per via inalatoria. [**The Factors of Prothrombinic Complex in Acute Poisonings following Inhalation**] *Med. d. Lavoro.* 1959, Jan., v. 50, No. 1, 13–24, 4 graphs. [18 refs.] English summary.

Blood clotting mechanisms were investigated in 16 cases urgently admitted to the *Clinica del Lavoro*, Milan, after exposure to unspecified amounts of certain toxic gases and fumes in 1957–8. 7 were affected by trichlorethylene, 1 by methyl chloride, 1 by ammonia, 1 by methane, 4 by carbon monoxide and 2 by fire smoke. In all cases serial estimations of the prothrombin index were made for some days. In the majority factor V and factor VII activities were also determined, and, in many of them, Howell's time, whole-blood clotting times in glass and siliconized glass by the Lee-White method, the prothrombin consumption test and the heparin tolerance test *in vitro*. Data from the tests and graphs and tables illustrate the trends. All cases showed some abnormality of clotting mechanisms during the first few hours, but while the first 12, including 2 of the subjects poisoned by carbon monoxide, showed delayed coagulation, the remaining 4 showed accelerated coagulation.

In the first 12, the prothrombin index continued to fall for 1–2 days, to 40–45%; during the next few days there was a slow upward trend, but in many cases normal values had not been reached 2–3 weeks later. A similar effect was shown by other tests, the activity of factor VII corresponding to that of prothrombin, the deficiency of factor V being less marked. Reasons discussed to explain these findings included the hepatotoxic effect of the 2 halogenated hydrocarbons and an anoxic effect on the liver cells by the other gases. The remaining 4 cases, 2 slightly poisoned by carbon monoxide and 2 asphyxiated by smoke, with no carboxyhaemoglobinaemia, showed increased activity of prothrombin factors, decreased Howell's time, decreased clotting times and an increased heparin tolerance. This effect was thought to be a non-specific reaction to the stress of the accident. *M. Patricia Fitzsimons*

HILL, W. H. & SMITH, R. C. **Analysis of Blood for Boron.** *Amer. Indust. Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 131–3.

ROUSH, G., Jr. **The Toxicology of the Boranes.** *J. Occupational Med.* Chicago. 1959, Jan., v. 1, No. 1, 46–52. [28 refs.]

The medical director of a company which manufactures these toxic compounds gives clinical findings as well as a review of toxicological data published since boron hydride poisoning was reported in 1951 [this *Bulletin*, 1952, v. 27, 173]. Those boranes which have the general formula $B_nH_{n+4}$ are stable and reactive, strong reducing agents, slightly soluble in water. They are used as fuels, selective reducing agents, fuel additives, bactericides, fungicides and initiators of rubber vulcanization and of ethylene, vinyl, styrene and acrylic polymerization.

Diborane $B_2H_6$, a gas, has an odour perceptible at 3 p.p.m. but the theoretical MAC is 0·1 p.p.m. A respiratory irritant rapidly hydrolysed to boric acid, it is also a systemic poison because in air a small quantity is converted to higher hydrides. Exposed animals show fall in blood pressure, decreased peristalsis and cortical activity, bradycardia, ventricular fibrillation and pulmonary oedema with haemorrhage. A few breaths give men transient respiratory distress quickly and headaches for which they do not always leave the area of work; occasionally symptoms recur after work together with chills and fever. In one study [*ibid.*, 1958, v. 33, 594] there were no abnormal chest findings but occasionally there was an altered pulse.

Pentaborane $B_5H_9$, a liquid, V.P. 185 mm. Hg. at 25°C., and Decaborane $B_{10}H_{14}$, a solid, V.P. 0·05 mm. Hg. at 25°C., may enter the body by inhalation, ingestion or through the skin. Similar in action, they may differ in degree and duration of effect because $B_5H_9$ hydrolyses faster. The boranes are much more toxic than boric acid which they resemble in toxic effects though urinary boron excretion is less and biliary greater. They are convulsive and hepato-renal poisons. Symptoms, sometimes delayed for 24 hours, included lightheadedness, drowsiness, headache and fatigue followed sometimes by twitching and marked muscle spasm. Twitching ceased in 24 hours and other symptoms within 3 days. A severe case of $B_5H_9$ poisoning with semi-coma, convulsions and hepato-renal damage recovered completely. The amine boranes, dimethylamine borane $(CH_3)_2NH.BH_3$, trimethylamine borane $(CH_3)_3N.BH_3$ and pyridine borane $C_5H_5N.BH_3$ hydrolyse slowly and are less toxic; the first parenterally is rapidly eliminated but by ingestion it is as toxic as $B_{10}H_{14}$ and a 10% aqueous solution locally produced skin and eye irritation in rabbits. Boron blood and urine analyses are difficult and often were negative after known over-exposure had caused symptoms.

Treatment is symptomatic. Eye and skin protection are necessary, and respirators where concentrations are high. Screening debars susceptible applicants with allergy or disease of the lung, heart, liver or kidney. Boranes may accumulate in the body or their effects may, and olfactory fatigue and the latent period may also contribute to poisoning. There is no monitoring device and no means of evaluating atmospheric concentrations. *M. Patricia Fitzsimons*

YEE, H. T., FOSDICK, L. B. & BOURNE, H. G., Jr. **Nitroglycerin and Nitroglycol Exposure in an Explosive Plant.** *Amer. Indust. Hyg. Ass. J.* 1959, Feb., v. 20, No. 1, 45–9. [11 refs.]

In this plant the sensitizer, called oil, used in the manufacture of dynamite and gelatin dynamite (gelly), contain 80% of nitroglycerin (NG) $C_3H_5(ONO_2)_3$ and 20% nitroglycol $C_2H_4(ONO_2)_2$. Data on the extent of atmospheric contamination in the explosives industry and on the toxicology of nitroglycol were found to be relatively meagre, though rumours persist that there might be a relationship between exposure to NG and heart disease. Atmospheric sampling in the powder line buildings, where the greatest potential exposure to oil is present, was restricted to 30 minutes between shifts because of safety requirements. Conditions, however, were considered to be representative. 42 airborne samples were collected by the midget impinger apparatus, the collecting medium being alcohol. Unsuccessful attempts had been made to develop a specific analytical method, including polarography and infrared spectrophotometry, for determining both NG and nitroglycol when mixed. Therefore, after preliminary treatments of the samples to eliminate inorganic nitrites and to hydrolyse organic nitrates, resulting in the release of nitrites, the concentration of nitrites in the form of $NO_2$ was colorimetrically determined. Atmospheric concentrations were expressed in 3 different ways: firstly, nitrites determined from hydrolysis of organic nitrates; secondly, as NG, computed by applying a hydrolysis factor of 1·662 moles of nitrites per mole of NG; thirdly, as nitroglycol, computed on an assumed basis of complete hydrolysis, *i.e.* 2 moles of nitrites per mole of nitroglycol.

General atmospheric concentrations by work locations, and also in both warm and cold seasons, are presented in tables, and show that measurable quantities of air-borne NG and nitroglycol were present in every case, though average values for NG in no instance exceeded its MAC of 0·5 p.p.m. In the powder line the concentrations of nitrites in p.p.m. were: distributor house 0·07, dynamite mixing house 0·63, gelly mixing house 0·45, dynamite hand packing house 0·22, dynamite machine packing house 0·43, gelly hand packing house 0·51, gelly stuffing house 0·51, dynamite case and gelly case houses 0·07. Outside the powder line, in the NG factory and the maintenance building the nitrites were 0·07 and 0·03 p.p.m. respectively. The weighted average daily exposure of 73 production workers in the NG factory and powder line, based where necessary on time-study and other observations, gave a similar range, *e.g.* the dynamite mixer 0·63 and the case house worker 0·07 p.p.m. The general average concentration for the powder line, 0·03 p.p.m., was used for the maintenance worker. The figures in the warm weather were 2, 3 and 4 times greater than in the cold, the greatest seasonal differences being in the distributor, gelly mixing and dynamite packing houses.

By applying equations derived by BRANDNER (*Indust. Eng. Chem.*, 1938, v. 30, 681) for vapour pressures of binary solutions, the vapour pressures at 20°C. of NG and nitroglycol in a 4 to 1 mixture were theoretically found to be 0·00028 and 0·01346 mm./Hg respectively. This suggested that the vapours from the oil had a nitroglycol to NG ratio of 48 to 1. Though ideally the samples should be chemically determined in quantities of NG and nitroglycol, were a method found to do this, it would seem reasonable to regard the organic nitrates analysed as all nitroglycol, the amount of nitroglycerin present being insignificant.

*M. Patricia Fitzsimons*

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BENES, V. & ČERNÁ, V. Akrylonitril: Akute Toxizität und Wirkungsmechanismus. [**Acute Toxicity and Action of Acrylonitrile**] *J. Hyg. Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 1, 106–16, 1 fig. [34 refs.]

Acrylonitrile ($CH_2 = CH - CN$) is being used to an increasing extent in the chemical industry because of its polymerization power and it is also employed as an insecticide in the fumigation of cereals. The mechanism of its toxic action is not yet known precisely, although this has been attributed to the setting free of hydrocyanic acid in the animal tissues.

In the present paper the authors describe experiments on mice and rats which were given the nitrile by mouth. There is a description of chemical methods employed for the determination in urine of thiocyanate which is considered to be derived from the free hydrocyanic acid in the tissues. A table sets out the results in the first experiments which were undertaken to determine the LD50 of different technical and chemically pure samples of acrylonitrile and a picture of the observed toxic effects. In subsequent experiments the animals were given sodium nitrite and sodium thiosulphate, which are antidotes to hydrocyanic acid, as well as acrylonitrile, in order to study the extent to which the mortality was altered. With mice it was found that the antidotes antagonized a dose of acrylonitrile 3 times as great as the upper limit of the LD50 which suggests that the mechanism of toxicity in these animals is the formation of hydrocyanic acid. In rats, however, the protective effect of the antidotes was much less and the amounts of thiocyanate found in the urine were calculated to represent only about 20% of the CN which might be released from the nitrile. The toxic action of acrylonitrile in rats would appear to be due in part to the molecule as a whole. *M. E. Delafield*

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BURKATZKAYA, E. N., IVANOVA, Z. V. & KRASNYUK, E. P. [**Labour Hygiene and the Health of Workmen engaged in the Production of Insecticides containing Hexachlorane**] *Gigiena i Sanitariya.* Moscow. 1959, v. 24, No. 5, 17–22. [10 refs.] [In Russian.]

The English summary appended to the paper is as follows:—

" An investigation of labour conditions during the production of insecticides containing hexachlorane has shown that the concentration of the compound in the air of workshops and auxiliary premises was from 0.001 to 0.034 mg/l. On the skin surface of the workers hexachlorane was found in amounts from 0.001 to 2.9 mg/cm² of the skin.

" Medical examination of the workers revealed pathological changes in the liver, nervous system and the blood, these increasing in proportion with the service record of the workers.

" The investigations served as a basis for elaborating measures aimed at improvement of labour conditions."

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SHIRAKAWA, M. **Experimental Studies on the Toxicity of Benzene Hexachloride (BHC) and Dichlorodiphenyltrichloroethane (DDT). II. Toxicity Tests by the Dust Inhalation of the Insecticides to Laboratory Animals.** *Kurume Med. J.* 1959, v. 5, No. 3, 190–97, 2 figs. **III. Histopathological Study.** *Ibid.*, 198–208, 16 figs. [10 refs.]

The author studied the effect on 10 rats and 49 mice of inhaling BHC powder (0·5% of gamma isomer, 4·5% of the other isomers, 85% bentnite and 10% of talc) and DDT powder (10% crystals of DDT diluted by 90% talc). The duration of the exposure varied from 5 to 120 minutes over a period varying between 1 and 91 days.

With BHC powder nose and eyes became irritated—in some rats there was bleeding from the eyes. Both rats and mice subjected to excessive exposure developed convulsions and died. Results of inhaling DDT were similar but less marked. Post-mortem there was congestion and haemorrhage in the lungs without gross changes in other organs.

Microscopically there was emphysema, slight atelectasis and alveolar pneumonia present in rats and mice after inhalation of BHC and DDT. Rats after BHC also showed slight hyperaemia of liver cells and some cloudy swelling of epithelial cells of nephritic ducts (5 out of 6 rats survived inhalation of BHC for 92 days). Mice showed similar changes after DDT. There was no change or only very little in the liver and kidney cells of animals that survived.

There follows in part III a detailed histological report of changes in the organs of rats and mice after absorption of BHC and DDT by various routes. The changes noted were much the same for both BHC and DDT (less marked for DDT) and differed little whether these chemicals were inhaled, ingested, injected intraperitoneally or had gained access through the skin.

The findings included:—

Lungs—congestion, oedema, atelectasis and haemorrhage.

Liver—occasionally slight fatty degeneration.

Kidneys—epithelial cells of ducts showed some cloudy swelling

Spleen, heart and muscles virtually no change.

Central nervous system—Nissl's bodies were collapsed and diffuse pigmentation of the nuclei was present.

[For abstract of Part I, see this *Bulletin*, 1959, v. 34, 353.] *T. O. Garland*

Apte, N. V., Khandetod, P. N. & Verkey, C. C. **Diazinon Poisoning.** *J. of J.J. Group Hosps. & Grant Med. College.* Bombay. 1958, Oct., v. 3, No. 4, 287–90.

5 cases of poisoning from diazinon (o.o.diethyl O-(2-isopropyl-4-methyl-6-pyrimidyl) phosphorothioate), an organo-phosphorus insecticide, are briefly described. 3 cases followed the swallowing of diazinon concentrate from a bottle. They vomited immediately. 2 had muscular fasciculations and one was diagnosed as having auricular fibrillation. These patients responded well to atropine alone. The other cases resulted from drinking from a container and a glass that had been contaminated with diazinon. No blood cholinesterase determinations were made.

[The diagnosis of auricular fibrillation is not convincing on the basis of the evidence provided.] *J. M. Barnes*

Gnoevaya, V. L., Krilova, M. I. & Russkikh, V. V. **[Assessment of a New Insecticide—Methylethylthiophose from the Standpoint of Food Hygiene]** *Gigiena i Sanitariya.* Moscow. 1959, v. 24, No. 5, 34–9, 3 figs. [In Russian.]

The English summary appended to the paper is as follows:—

"Methylethylthiophose is a new insecticide from the group of organic phosphorus compounds and is recommended for the use instead of thiophose. When employed for agricultural purposes, the proportion of this poisonous matter in the final product is intended to reach 30%.

"Chronic poisoning tests have shown that for warm-blooded animals methylethylthiophose is more toxic than the thiophose.

"Because of its higher toxic properties, as compared to the thiophose now permitted for use, the application in agriculture of the new compound—methylethylthiophose is inadvisable from sanitary and hygienic viewpoint."

Petty, C. S., Hedmeg, A., Reinhart, W. H., Moore, E. J. & Dunn, L. F. **Organic Phosphate Insecticides—a Survey of Blood Cholinesterase Activity of Exposed Agricultural Workers in Louisiana, 1957.** *Amer. J. Pub. Health.* 1959, Jan., v. 49, No. 1, 62–9, 3 figs. [10 refs.]

"Blood specimens from 245 farmers, crop-dusting pilots, crop insect checkers, insecticide mixers, tractor drivers, and other agricultural workers were analyzed for blood cholinesterase activity during the 1957 cotton crop treatment season in Louisiana. No instance of subclinical organic phosphate insecticide poisoning was discovered in this survey, although all persons contributing blood samples were exposed in varying degree to these toxic agents. During this same season, only four cases of proved overt organic phosphate poisonings were encountered among agricultural workers in Louisiana."

Murphy, S. D., Anderson, R. L. & Dubois, K. P. **Potentiation of Toxicity of Malathion by Triorthotolyl Phosphate.** *Proc. Soc. Exper. Biol. & med.* 1959, Mar., v. 100, No. 3, 483–7. [10 refs.]

Triorthotolyl phosphate (TOTP), an inhibitor of aliesterases in the rat, has been shown to potentiate the toxicity of the relatively non-toxic organo-phosphorus insecticide malathion.

Doses of TOTP 10 mgm./kgm. (intramuscularly, 3 times in 5 days), 110 mgm./kgm. (cutaneously once) or 110 mgm./kgm. (intraperitoneally) reduced the LD50 of malathion from 1100 mgm./kgm. (intraperitoneally) to 125, 12·5 and 8·2, respectively. In these doses TOTP alone was without effect on the rats. The ability of the tissues of the TOTP-treated rats to detoxify malathion was demonstrated by *in vitro* tests. This observation that the toxicity of an insecticide may be potentiated by quite unrelated compounds which might be ingested from a variety of sources is discussed. *J. M. Barnes*

Hobbiger, F., O'Sullivan, D. G. & Sadler, P. W. **New Potent Reactivators of Acetocholinesterase inhibited by Tetraethyl Pyrophosphate.** *Nature.* 1958, Nov. 29, v. 182, 1498–9.

Certain nucleophilic reagents restore the activity of acetocholinesterase inactivated by interaction with tetraethyl pyrophosphate. These compounds, which are of importance in combating organophosphate poisoning, react by displacing the phosphoryl group from the enzyme.

A number of synthetic oximes have been tested for affinity for acetocholinesterase, interaction with tetraethyl pyrophosphate, and effectiveness in restoring the activity of acetocholinesterase inhibited by tetraethyl pyrophosphate.

The most powerful reactivators so far encountered are structurally related to pyridine. Monoximes and dioximes of bis-pyridinium ions are all considerably more potent reactivators than pyridine-2-aldoxime methiodide, although they are derivatives of the less active pyridine-4-aldoxime methiodide. A considerable gain in activity is also obtained by terminal halogen substitution in the alkyl side chain. It appears that a conjugative connexion between the quaternary nitrogen and an oxime or hydroxamic acid group is essential for high activity. *J. H. Birkinshaw*

FOURNEL, J. Action antidote de l'iodométhylate de l'α-pyridylaldoxime vis-à-vis des intoxications expérimentales provoquées par les insecticides organophosphorés. **[The Protective Effect of Pyridine Aldoxime Methiodide in Experimental Poisoning by Organo-phosphorus Compounds]** *C.R. Soc. Biol.* 1957, v. 151, No. 7, 1373–7. [Refs. in footnotes.]

Although atropine appears to be the most effective antidote in poisoning by organo-phosphorus compounds, it only counteracts the muscarinic effects and exerts no action against the complexes formed between the enzymes and their inhibitors. These complexes are destroyed by certain derivatives of hydroxylamine and *in vitro* the latter reactivate cholinesterases but unfortunately they are inert *in vivo*.

In 1955 WILSON and GINSBURG (*Biochim. et Biophys. Acta*, 1955, v. 18, 168) demonstrated that pyridine aldoxime methiodide reactivated *in vitro* the enzymes inhibited by DFP (di-isopropyl fluorophosphonate) and paraoxon, and also protected animals against lethal doses of these poisons. The author decided to test the antidotal effect of PAM (pyridine aldoxime methiodide) in experimental poisoning of mice and rabbits by parathion, endothion and demeton-methyl (metasystox). The original should be consulted for more detail concerning the experimental methods and the results of the tests.

It is shown that PAM counteracts the neuromuscular block which gives rise to respiratory paralysis and death and it does this in association with atropine. In parathion intoxication the red cell esterases regenerate very slowly, but in rats poisoned with this compound and treated with PAM the regeneration is more rapid. PAM is strongly indicated in poisoning by endothion because in this instance the nicotine effects are predominant.

Finally a strong plea is made for the use of PAM in conjunction with atropine in the therapy of intoxications by organo-phosphorus compounds. *P. J. R. Challen*

DAVIES, D. R., GREEN, A. L. & WILLEY, G. L. **2 - Hydroxyiminomethyl - *N* - Methylpyridinium Methanesulphonate and Atropine in the Treatment of Severe Organophosphate Poisoning.** *Brit. J. Pharmacol. & Chemotherapy.* 1959, Mar., v. 14, No. 1, 5–8. [13 refs.]

The soluble methanesulphonate of this oxime (P2S), with atropine, was effective before or after poisoning by sarin or ethyl pyrophosphate, though there was species variation. It was as effective as the relatively insoluble iodide of the oxime (P2AM) when tested against sarin poisoning. P2S was prepared by boiling 2-hydroxyiminomethylpyridine with methyl methanesulphonate in benzene; its MP was 155°; it was dissolved in water, *p*H being adjusted to 7·4 just before injection. Atropine sulphate (17·4 mgm./kgm.) was injected in the same solution as the oxime. P2S was given intramuscularly in volumes of 3 ml./kgm. body weight to mice and 1 ml./kgm. to rats, guineapigs and rabbits. Sarin (*iso*propyl methylphosphonofluoridate) or ethyl pyrophosphate was given subcutaneously in saline in volumes of 10 ml./kgm. to mice, 1 ml./kgm. to rats and guineapigs and 0·5 ml./kgm. to rabbits.

When 30 mgm./kgm. of P2S was given 1 minute after poisoning, the LD50 of ethyl pyrophosphate was raised 20-fold in mice, guineapigs and rabbits, and 5-fold in rats, and the LD50 of sarin was raised 40-fold in guineapigs, 4-fold in mice and less in rats; when given 10 minutes before poisoning, the LD50 of ethyl pyrophosphate was raised 20 to 50-fold in each species, and the LD50 of sarin was increased 70–100 times in rabbits and guineapigs and 3–4 times in rats and mice. Increasing the therapeutic dose produced no proportionate increase in effect in mice poisoned by sarin, but in rats did so slightly. Prophylactically, however, increasing the dose increased the effect and also the duration of protection: groups of 25 rats and mice were given 120, 60, 30 or 15 mgm./kgm. of P2S, and after intervals the rats were given 0·75 mgm./kgm. of sarin (5·4 × LD50) and the mice 1·2 mgm./kgm. (4 × LD50); the 120 mgm./kgm. still gave some protection after about 2 hours and though the optimum interval was greater at the highest dose, a 10-minute interval "almost always gave nearly optimal results".

In accidental insecticide poisoning it would probably be practicable to inject intramuscularly a therapeutic dose of 30 mgm./kgm. of P2S, *i.e.* about 2 gm./man in about 5–6 ml. water, rather than the large intravenous volume of the iodide. Prophylactically, regular injection of the methanesulphonate is unlikely to be widely applicable. *M. Patricia Fitzsimons*

FRADÀ, G. & GUCCIARDI, G. Ulteriori ricerche sugli effetti di farmaci neuroplegici nell'intossicazione sperimentale da esteri fosforici. **[Further Investigation on the Effects of Neuroplegic Drugs in Experimental Phosphoric Esters Poisoning]** *Med. d. Lavoro.* 1959, Feb., v. 50, No. 2, 83–90. [21 refs.]

The English summary appended to the paper is as follows:—

"Previous investigations by the Authors showed that Chlorpromazine has a protective effect on acute poisoning due to phosphoric esthers (*Malotox-P20* [a mixture of malathion and parathion]): it relieves or even eliminates nicotine-like symptoms, prevents acute pulmonary edema and increases the survival of the animals. The action of other neuroplegic drugs on the same poisoning was therefore tested: Promazine (dimethylamino-propyl-N-phenothiazine chlorhydrate) and perphenazine (1-(2-hydroxyethyl)-4-3-(2-chlor-10-phenothiazyl) propylpiperazine), both as such and associated with ACTH and atropine. The results show that neither promazine nor perphenazine interfere with nicotine-like symptoms, as on the contrary does chlorpromazine; however they show a certain degree of anti-bronchospastic effect and prevent acute pulmonary edema, no effect is shown on the survival of the animals.

"The association of promazine and ACTH and respectively of perphenazine and ACTH is found less effective than the hormone alone, while the contrary was previously observed with the association of chlorpromazine and ACTH. The association of promazine, ACTH and atropine and respectively perphenazine, ACTH and atropine are much less effective than the association chlorpromazine, ACTH and atropine as previously tested."

SUSKIND, R. R. **Occupational Skin Problems. I. Mechanisms of Dermatologic Response.** *J. Occupational Med.* Chicago. 1959, Jan., v. 1, No. 1, 39–45, 2 figs. [17 refs.] **II. Methods of Evaluation for Cutaneous Hazards.** *Ibid.*, Feb., No. 2, 119–24, 3 figs. [15 refs.]

SUSKIND, R. R. **Occupational Skin Problems. III. Case Study and Diagnostic Appraisal.** *J. Occupational Med.* Chicago. 1959, Apr., v. 1, No. 4, 230–36.

GROSDANOV, A. Berufsbedingte Ekzeme und Hautentzündungen durch Raupen der *Plodia interpunctella.* [**Occupational Eczemas and Inflammation of the Skin by Caterpillars of the Species** *Plodia interpunctella*] *Berufsdermatosen.* Aulendorf. 1959, Feb., v. 7, No. 1, 30–35.

Of 113 girls sorting and packing shelled walnuts no less than 39 complained of skin trouble. In 9 cases a diagnosis of "Eczema professionale" was made and in another 15 of "Dermatitis professionalis allergica". The rest, without presenting any kind of eczematoid reaction, complained of pruritus, palmar erythema, dermographism and the like.

The moth *Plodia interpunctella* attacks all kinds of dried fruit and vegetables. The larva is said to crawl over the dry shell of the walnut until it finds a weak spot in the joint near where the stalk used to be, and then to gnaw its way into the shell in order to attack the kernel. The kernel shrivels up and the space between it and the shell becomes filled with faeces, bits of cocoon silk and debris. There are sometimes large quantities of this dust. Unfortunately apart from the statement that the moth lays 40–350 eggs and the larva has a few sparse hairs the author gives no useful description of the insect.

Some of the workers had already experienced minor degrees of skin irritation; but it was not till the summer of 1954 when a high proportion of nuts were infested that the trouble developed on an important scale. This did not happen until 2–3 weeks after a heavily infested consignment of nuts had been disposed of: presumably because of the allergic sensitization provoked by the massive exposure would take about this time to develop.

An alcoholic extract of the larva and alcoholic, watery and acetone extracts of its faeces were used for patch testing. The 9 cases of "Eczema professionale" and of the cases of "Dermatitis professionalis allergica" all 12 that were tested, all reacted to the watery extract of faeces, but none of the 14 controls. The other extracts proved less satisfactory.

*J. H. Twiston Davies*

GONZÁLEZ BENAVIDES, J. Sporotrichose als Berufskrankheit in Töpfereibetrieben. [**Sporotrichosis as Occupational Disease in Potteries**] *Berufsdermatosen.* Aulendorf. 1959, Feb., v. 7, No. 1, 22–9. [16 refs.]

The author reports 16 cases of sporotrichosis among labourers engaged in packing pottery, most of them using zacate, the hay derived from a forage plant widely distributed in Mexico.

Since the substitution of cardboard and paper for zacate 5 years ago there have been no more cases.

*J. H. Twiston Davies*

HOLZMANN, H. "Vogelaugenartige" Hautveränderungen bei Arbeitern in der zinnverarbeitenden Industrie. [**"Pigeon-Eyes"-like Skin Alterations in Subjects occupied in Tin Industry**] *Berufsdermatosen.* Aulendorf. 1959, Feb., v. 7, No. 1, 36–41, 1 fig. [12 refs.]

From the descriptions provided, it is quite impossible to conjure up a convincing picture of any kind of bird's eye. The lesion seems to have been quite banal, and in appearance and clinical course can hardly be distinguished from the "chrome-hole" with which most of us are familiar. The offending material in this case was thought to be zinc chloride used as a flux for soft soldering. *J. H. Twiston Davies*

IPPEN, H. Berufsbedingte Hautveränderungen durch Phenothiazin-Derivate. [**Occupational Alterations of the Skin by Phenothiazine Derivatives**] *Berufsdermatosen.* Aulendorf. 1959, Feb., v. 7, No. 1, 12–21. [61 refs.]

Contact dermatitis produced by drugs of the phenothiazine group constitutes an important occupational hazard in the nursing, pharmaceutical and medical professions.

The author believes that it is because contacts are so varied and hazards so numerous that patients cannot always tell what is irritating their skin or tend incorrectly to incriminate some contact other than the one responsible.

Phenothiazine itself is well known as a remedy for ascariasis in sheep; the derivatives promazine, chlorpromazine, perphenazine, diethazine and promethazine are used as tranquillizers for *homo sapiens*. The patient may get a non-specific erythematous rash by ingestion or he may become light-sensitive and produce an exaggerated sunburn reaction. It is, of course, possible for a patient to sensitize his skin from without but this is more likely to happen to the nurse or dispenser.

Exogenous sensitization may lead to an ordinary allergic contact dermatitis; but it is supposed to be rather characteristic of it that only the exposed parts are attacked—very often with a sharp border at the sleeve edge and collar.

In some cases exposure to light seems to be essential to the reaction for in such a case the patient can handle chlorpromazine with impunity as long as he stays in the dark.

The ordinary form of covered patch test cannot be relied on to demonstrate allergy. The author recommends treating an area on the back 15 cm. × 1 cm. with 1% chlorpromazine for 24 hours and then exposing a number of strips crossing the treated area at right angles, to UVL for anything between 1 minute and 16 minutes. Provided the test is not upset by the fact that chlorpromazine itself is an excellent sunscreen, it may be possible to show that the threshold for UVL erythema has been lowered by pretreatment of the skin with chlorpromazine. This would imply that the patient's skin reacted abnormally to the drug and justify a diagnosis of occupational dermatitis.

*J. H. Twiston Davies*

KILE, R. L. & QUIGLEY, J. A. **Skin Eruptions of Workers in a Uranium-Processing Plant.** *Arch. Dermat.* 1959, Apr., v. 79, No. 4, 383–9, 3 figs.

The process is described as follows. Uranium ore is digested with nitric acid to produce uranyl nitrate. Then water is used "to wash out impurities" [presumably rather to extract the uranyl nitrate which of course is highly soluble]. After concentration the uranyl nitrate is calcined to uranium trioxide, next reduced by means of hydrogen to the dioxide, and then converted to uranium tetrafluoride which, having been pulverized, is reduced in a furnace and cast in graphite moulds into metallic ingots. The workmen wear special clothing, bathing and changing back for lunch and to go home. The special clothing is washed and a worthwhile amount of uranium extracted from it. Traces of the detergent used are neutralized by sodium acid fluoride. Superfatted soap is supplied for the bathing and clogs are worn to prevent the spread of tinea pedis.

Some general dryness of the skin [perhaps "asteatosis" in the list of dermatological diagnoses] having been complained of, the laundry process was investigated. On one occasion it was found that the rinse period had been reduced and on another that the laundry man had mistaken ounces for pounds in calculating the quantities of both detergent and neutralizer. Apart from a couple of burns by hydrogen fluoride no skin lesion specifically attributable to the main process was observed. There were a number of cases accepted as contact dermatitis due to "oil, chemicals employed in the plant, defatting agents, etc.". But the authors consider that they have had less trouble than usual from the tendency of workmen to "blame their work for problems that have no connection with it"; and they attribute this to the confidence engendered by an impressive routine of precautionary testing procedures.

*J. H. Twiston Davies*

NOLAN, W. E. & BLOCK, S. **Radiation Hazards associated with Dental Roentgenography.** *Amer. Indust. Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 118–20, 4 figs.

BORGOLTE, W. Die Aufgaben des öffentlichen Gesundheitsdienstes im Strahlenschutz. **[The Function of the Public Health Service in Protection against Radiation]** *Öffentl. Gesundheitsdienst.* Stuttgart. 1959, v. 21, No. 1, 10–15.

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# Atmospheric Pollution

DEPT. SCIENT. & INDUST. RES. **The Investigation of Atmospheric Pollution. Research and Observations in the Year ended 31st March, 1957.** Thirtieth Report. pp. iv + 136. 1959. London: H.M. Stationery Office. [7s. 6d.]

Most of this publication is devoted to tables of data on atmospheric pollution obtained during the year ending March 31, 1957, by the 351 bodies cooperating with the Department of Scientific and Industrial Research. These cooperating bodies—Local Authorities, industrial undertakings and other institutions—operate at their own expense 993 deposit gauges, 1,115 monthly sulphur dioxide instruments of the lead peroxide type, 140 daily sulphur dioxide (volumetric) outfits, 187 daily smoke filters and 6 automatic smoke filters. The data are set out in great detail. For example, the measurements of deposited matter at very many points are given for the summer and winter months as undissolved matter (divided into tar, ash and other combustible matter) and dissolved matter (Ca, Cl, $SO_4$ and total) in grammes per 100 square metres per month. Determinations of suspended matter (smoke) and sulphur dioxide are recorded in similar fashion by monthly, seasonal, week-day, week-end and sometimes hourly averages.

There is an interesting report by the Director of Fuel Research on the Investigation of Atmospheric Pollution. In this there is a general account of the data provided by the cooperating bodies with tables that set out the high, average and low values for pollutants obtained at different sites. The researches carried out at the Research Station were on the measurement of smoke from boilers and furnaces from a distance by means of a new instrument which has been patented; a new simple indicator which enables the fireman to detect from the firing platform when smoke is being produced by a particular boiler; the combustion of the combustible constituents of the exhaust gas from petrol engines in a catalytic chamber which replaces the normal silencer; the measurement of smoke in exhaust gas; the identification and determination of toxic and irritant substances in exhausts; removal of sulphur compounds from flue gas and investigations of some problems of domestic heating.

Experimental work is also being carried out at the University of Sheffield on the abatement of smoke from metallurgical furnaces and at Imperial College, London, on the dispersion of chimney gases in the atmosphere. Both these problems are being investigated as part of the programme of the Fuel Research Board.

*M. E. Delafield*

UNITED STATES PUB. HEALTH SERVICE. **The National Conference on Air Pollution, Washington, Nov. 18, 1958. (a) Status Report to the Nation** [BURNEY, L. E.]. *Amer. Indust. Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 153–7. **(b) Reports and Recommendations of Discussion Groups** [MCCABE, L. C., KENNEDY, H. W. & ROGERS, S. M.]. *Ibid.*, 157–66.

FOITZIK, L. Zusammensetzung und optische Eigenschaften des natürlichen atmosphärischen Staubes. [**Composition and Optical Characteristics of Natural Atmospheric Dust**] *Staub.* Düsseldorf. 1959, May 1, v. 19, No. 5, 197–200, 7 figs. [15 refs.]

The English summary appended to the paper is as follows:—

"Following a brief survey of the use of the term "dust" in meteorology, the article deals with the most varied manifest forms, the origin, the composition and the size distribution of the natural atmospherical dust. The optical characteristics of vapour or mist and their dependency from the size distribution of the particles are examined by means of the light dispersion."

EFFENBERGER, E. Vergleichsmessungen mit verschiedenen Staubmessverfahren (Auffanggerät nach Löbner, Haftfolienmethode nach Diem, Registriermethode nach Effenberger). [**A Comparison of Different Dust Measuring Devices. (Löbner's Collection Apparatus, Diem's Adhesive Foil Method and Effenberger's Recorder)**] *Staub.* Düsseldorf. 1959, Feb. 1, v. 19, No. 2, 44–6, 7 figs.

The 3 systems were set up on the roof of a building in Hamburg and tested in atmospheric pollution for one year. The adhesive foil was changed weekly, and the flask of the collector monthly. The recorder [EFFENBERGER, this *Bulletin*, 1958, v. 33, 138] ran for 14 days.

Some measure of correlation was established between the results from the recorder and those from the average of at least 5 adhesive foils. Löbner's apparatus gave indications which did not fall into line with the other 2 methods.

*C. N. Davies*

JENEY, E. & SZENDREY, S. Untersuchung der Metallverunreinigung der Luft mit Hilfe der papierchromatographischen Methode. [**The Detection of Metallic Contaminants in Air by means of Paper Chromatography**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1958, Sept.–Oct.–Nov.–Dec., v. 4, Nos. 5/6, 249–53.

The air of a Hungarian city was sampled for several days at a time at a number of stations and analysed for silica, iron, nickel and lead. The general pollution reached maximal values in October, the second half of March and the second half of April, but the percentage of silica changed very little. The traces of metals probably originated from internal combustion engines and machines.

A table gives full details of the 18 samples which were studied.

*C. N. Davies*

ROYAL SOC. PROMOTION HEALTH J. 1959, Jan.–Feb., v. 79, No. 1, 4–24. **Chronic Bronchitis and Air Pollution** [LAWTHER, P. J.], 4–9, 2 figs. [11 refs.] **Bronchitis and Air Pollution** [BURGESS, S. G. & SHADDICK, C. W.], 10–22, 5 figs. [12 refs.] Discussion 23–4.

The first paper is an admirable review of the problems which face the investigator into the relation between chronic bronchitis and air pollution. No satisfactory pathological definition has yet emerged, and the author falls back on OSWALD's clinical syndrome as a definition. On air pollution he shows the lack of qualitative analysis of its constituents, and research has so far been concerned with deposited and suspended matter and presence of gaseous sulphur dioxide. He divides pollution into acute, sub-acute, and chronic. In the acute form it is found that it is a replacement of water particles by smoke rather than condensation of water vapour round oily soot particles. Often the presence of fog is not associated with a high level of smoke. The sub-acute occurs frequently on winter evenings for short periods, and the chronic is the normal dirty air which is usually present in towns during the winter in Great Britain. The author points out the necessity for investigation into the size of the particulate matter which probably has a marked effect on its penetration into the bronchioles.

Turning to the relationship between pollution and bronchitis, he points out the possible pitfalls that may occur in mortality from chronic bronchitis and densely populated areas, but REID's investigation done on postmen who are a homogeneous selection shows clearly that the relationship does occur. An investigation which is being undertaken at St. Bartholomew's Hospital, London, shows that episodes of acute pollution lead to deterioration in chronic bronchitis, but this is not necessarily associated with fog. This investigation is continuing. The paper is an excellent short summary of modern knowledge.

The second paper consists of 2 parts. In the first there is a consideration of possible impurities. The sources of sulphur and nitrogen oxides are examined. The difficulties of estimation are emphasized and it is pointed out that an increased mortality is associated with a level of $SO_2$ less than is thought to be injurious. It is suggested that a secondary reaction may be present producing a more toxic material and $NO_2$ may by itself, or as a result of combination be important. The difficulties of estimation are emphasized, especially that at least 4-hour readings are scientifically necessary though at present impracticable. The percentages of various constituents are never stated. 7 stations have been equipped in the London area. Figures are given showing that the average amount of $SO_2$ has decreased during the past 4 years, but the concentration of acid gases has been maintained. A vivid impression of the difficulties is conveyed.

The second part is on the mortality from chronic bronchitis. The population at risk is considered from various aspects. It appears that long-term residence in London leads to higher risk of death from chronic bronchitis, but differences between various areas is slight. 4 episodes of fog, as usually defined, occurred in the 3 winters 1954–5 to 1956–7, and correlated with a 7-day moving average of deaths, but only in December 1956, and December 1957 was the rise in bronchitic death-rate very marked. The constituents of air pollution in the 2 episodes were different, and in the first the mortality rise hit mainly old people, while in the second this difference was much less apparent, but these 2 facts were not necessarily cause and effect. Temperature variations are also associated with increased mortality. Much interesting information is given in this paper, but the impression received is that even the surface of the many problems has only been scratched.

*Discussion*

After these 2 excellent papers the subsequent discussion was rather ineffective. Several speakers dragged in smoking and radio-activity. The latter was quickly disposed of by the statement that atmospheric radio-activity was higher in rural granite areas in Cornwall and Scotland. W. C. Turner suggested that hydrochloric acid produced by stack flues might be important and the irritant nitrosyl chloride might be produced by its interaction with nitrogen oxides. R. E. Waller reported that in addition to $SO_2$, sulphuric acid and sulphur trioxide might be present but could be neutralized by ammonia. S. G. Burgess pointed out that some of the hydrochloric acid produced by the relatively low temperature domestic fires was converted into ammonium chloride.

*F. H. Young*

Wildführ, G. Staubproblem in der Grossstadt. **[Air Pollution in Large Cities]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1958, Sept.–Oct.–Nov.–Dec., v. 4, Nos. 5/6, 241–8, 2 figs.

This is a general review of the pollution in modern cities which derives principally from industry, transport and domestic heating. The first 2 sources are increasing alarmingly. Many authors are cited and statements made but there is no documentation.

Sulphur dioxide and sulphuric acid arise from the sulphur content of coal, gas and diesel oil. Industrial sources emit ammonia, chlorine, hydrochloric acid, nitric acid and hydrofluoric acid. All these substances are irritant and respiratory poisons.

Carbon monoxide, produced by imperfect combustion, has a toxic limit between 0·01 and 0·02% by volume. Since, unlike sulphur dioxide, it is lighter than air, it is rapidly diluted but concentrations up to 0·046% have been recorded in heavy traffic.

Dust and smoke particles are most harmful to man when about 1 micron in size. Carcinogenic dusts include compounds of arsenic, beryllium, chromium and nickel. Chimney smoke contains carcinogens.

The spread of pollution is conditioned by microclimatological and by meteorological factors; vertical and horizontal spread are equally important. In cities traffic pollution is significant mainly at street level, domestic fires have an appreciable effect to a height of 20 m. and industrial pollution to 50 m.

The heaviest burdens of pollution are found at low wind speeds and high relative humidities. Warm air masses carry more dirt then cold; the source and the route over the continent determine the dust load of a travelling air mass.

Woods and parklands exert a filtering effect which is enhanced by warmth and moisture.

Town-planning authorities should bear the following points in mind. Green areas are needed for air purification. Railways and industry should be sited away from residential areas and separated from them by green belts. Buildings should be sited to allow free circulation of air around them. Main traffic routes should be to leeward of a city.

Spores of tetanus and other organisms occur in town dust. Figures are given for the occurrence of 7 species of *Clostridium* which were collected on 25 sampling plates exposed in Leipzig. *C. N. Davies*

# Sanitation

## GENERAL

THOMSON, W. O. & BROWN, J. S. **Sanitary Accommodation on Building Sites.** *Med. Officer.* 1959, Apr. 10, v. 101, No. 15, 200–201.

In this short paper there is an account of an enquiry which was made into the hygiene and standards of sanitary accommodation provided for the workmen on all the 45 building sites registered with the local authority in the Central Division of Glasgow. The points of the enquiry were the number and type of sanitary accommodation, its cleanliness, privacy and comfort and accessibility. The findings of the enquiry are clearly described. In Great Britain the building industry employs over one and a quarter million people and "It would appear from this small enquiry that one of the amenities in need of improvement is that of the sanitary facilities," which are all too often of unsatisfactory standard much lower than that provided in factories and warehouses.

Present legislation is inadequate for the control of sanitary accommodation for building employees in some types of work and at the present time all that can be done is the maintenance of vigilant local authority inspection and efforts of persuasion.

*M. E. Delafield*

## WATER AND SWIMMING BATHS

*(Including the Bacteriology of Water Supplies)*

ENGELBRECHT, R. S. & MORGAN, J. J. **Studies on the Occurrence and Degradation of Condensed Phosphate in Surface Waters.** *Sewage & Indust. Wastes.* Wash. 1959, Apr., v. 31, No. 4, 458–78, 7 figs. [13 refs.]

ETINGER-TULCZYNSKA, R. **The Effect of Various Water Bacteria on the Growth of** *Escherichia coli* **I in MacConkey's Broth at 37° and 42°.** *J. Applied Bact.* 1958, Dec., v. 21, No. 2, 174–9.

Mixed cultures of *E. coli* I and various other bacteria isolated from water were studied. A streptomycin resistant *E. coli* I strain was used for ease of differentiations from other organisms. Species of *Achromobacter*, *Micrococcus*, *Proteus* and *Pseudomonas* did not significantly affect growth of *E. coli*. *Achromobacter* and *Micrococcus* died out, *Proteus* survived in small numbers and *Pseudomonas* multiplied in the 24-hour incubation period. Other coli-aerogenes bacteria *Klebsiella* [*Cloaca*] *cloaceae*, *K. aerogenes* and *Citrobacter freundii* did, however, cause some retardation or inhibition of growth of *E. coli* I at 37°C. especially when initially present in very much larger numbers, although in all cases *E. coli* I was still recoverable. At 42°C. the interfering action of *C. freundii* was much less marked. When mixtures of several organisms were grown in association with *E. coli* I the strongest inhibitor exerted its usual effect.

The effect of this interference with growth of *E. coli* I on its ultimate recovery from a sample will depend on the efficiency of the technique used to confirm the presence of *E. coli* I in the primary culture.

*E. Windle Taylor*

ECKER, R. E. & LOCKHART, W. R. **A Rapid Membrane Filter Method for Direct Counts of Micro-organisms from Small Samples.** *J. Bacteriology.* 1959, Feb., v. 77, No. 2, 173–6, 2 figs.

This is another method of obtaining direct counts of micro-organisms by means of membrane filtration. When filtered the cells are distributed over a surface of known area. The cells are stained with 0·1% acid fuchsin and counted by direct observation through the high powers of the microscope after the filter has been made transparent by application of immersion oil.

The accuracy of the results depends very much upon a uniform distribution of the bacterial cells over the filter area. Sample volumes as small as 50–100 $\mu$l. distributed with a microlitre pipette are sufficient if filter areas of 2·5–3·0 mm. diameters are used. It was found that the volume filtered should not be less than twice the cube of the diameter of the filtering area.

Checks were made on the efficiency of the method with 3 different concentrations of *Escherichia coli* culture suspension and comparison was made between total counts and viable counts of an *E. coli* culture. The results of the latter experiment revealed an important point, namely that the membrane filter counts of a culture up to 12 hours (the period of the experiment) were virtually identical with the corresponding viable counts indicating the accuracy of the direct count regardless of the physiological age of the cells.

The method requires no elaborate apparatus nor complex manipulation and there is a significant saving in time and materials.

*E. Windle Taylor*

MEYER, R. Zur Einfuhrung des Salmonellenquotienten in die bakteriologische Wasseruntersuchung. **[On the Determination of the Salmonella Quotient in the Bacteriological Examination of Water]** *Arch. f. Hyg. u. Bakt.* 1959, Apr., v. 143, No. 3, 221–40, 12 figs.

Samples of deep well water from Aurich were inoculated with suspensions of *Salmonella typhi* and *Salm. paratyphi B* and incubated at 7°C., 20°C. and 37°C. The surviving bacteria were then estimated after 24 hours. With *Salm. typhi* a bactericidal effect was noticed at all temperatures and in samples from all stages of the purification process. In the case of *Salm. paratyphi B* there was a tendency for the bacteria to multiply in the raw and partially purified water in the samples incubated at 37°C. only. The opposite effect was seen in the filtered water. This was thought to be associated with the iron content, the raw water being rich in iron. The bactericidal effect could not be correlated with any particular chemical factor. The natural anti-bacterial power of the water was found to vary from time to time and it is suggested that estimation of the "Salmonella quotient" (*Keimverminderungsquotient*) should be regarded as a necessary supplement to the usual methods of water examination.

*E. Windle Taylor*

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# Food and Nutrition

## GENERAL

MULDER, T. De voeding in Nederland. **[Food in the Netherlands]** Reprinted from *Voeding.* 1959, v. 20, No. 3, 105–16, numerous charts.

This is an account, with detailed lists and graphs, of annual quantities of food delivered, food values per head of different products and daily intake per head in calories and nutrients in the Netherlands between 1938 and 1957.

There are short descriptive notes on the tables.

The tables, and the captions to the 31 graphs, are presented in both Dutch and English.

*H. J. O'D. Burke-Gaffney*

VOEDING [Reprinted from.] 1958, v. 19, No. 8, 393–539, 20 charts. [Essential points in English.] Onderzoek naar de voeding en voedingstoestand van schoolkinderen in tien grote steden in 1951 en 1952. **[Survey of the Nutrition and Nutritional State of School Children in Ten Large Cities in 1951 and 1952.]** [DUTCH NUTRITION COUNCIL.]

This long publication contains the results of a survey of the nutrition of school children in 1951 and 1952 in the cities of Amsterdam, Rotterdam, the Hague, Utrecht, Haarlem, Eindhoven, Groningen, Enschede, Arnhem and Maastricht. The summary of the findings is translated into English as also are the particulars of the 20 charts, 72 tables and 11 appendices.

Random samples of 7-, 8- and 9-year-old boys and girls from 3 different income groups were investigated to determine the food intake and nutritional state of the children. The tables set out the amounts of the various dietary constituents provided for these different groups by age, sex and income class. The nutritional state was assessed clinically, by biometrical determinations and blood examinations for concentration of haemoglobin, vitamin A, ascorbic acid and carotenoids.

There is very full description and discussion of the findings. In general it may be said that the differences in nutritional status which were found to exist "were mainly to the disadvantage of the lower classes and often also to the disadvantage of children of large families in all income groups." Although these differences need not be attributed solely to nutrition since social and hygienic factors also may play a part nevertheless the food eaten by the lower income groups is inferior in nutritional value to that consumed by the higher income groups. This inferiority lies chiefly in a lower consumption of milk, meat, fruit and vegetables.

"It may therefore be concluded that a not inconsiderable group of the population in 1951 and 1952 was sustained by an insufficiently balanced diet."

*M. E. Delafield*

## FOODSTUFFS

### *Composition and Bacteriological Control*

MORAN, T. **Nutritional Significance of Recent Work on Wheat, Flour and Bread.** *Nutrition Abstracts & Reviews.* 1959, Jan., v. 29, No. 1, 1–16, 1 fig. [Numerous refs.]

This is a valuable review, which collects together a large number of recent studies on the chemical composition of wheat, flour and bread. A short introduction gives a useful summary of the types of breads consumed in Great Britain in the last 10 years. This is followed by an account of attempts to improve the quality of wheat by the use of fertilizers. Grains with a protein content as high as 21% have been obtained by persistent spraying of the crop with nitrogen fertilizers. There are practical difficulties in applying chemicals in this manner and in general feeding trials have shown that orthodox fertilizer treatments bring about only small rises in nutritive value.

A useful table and figure give the distribution of members of the B group of vitamins in the whole grain and in flours of various extraction. It would appear that pyridoxine, pantothenic acid, folic acid and biotin are distributed primarily in the scutellum, embryo and aleurone layer of the grain and that losses occur in milling low extraction flours which are of a similar order to the well-known losses of thiamine.

A table gives a summary of the content of tocopherols in various wheat products and their vitamin E activity is discussed.

A long section on proteins is concerned primarily with attempts to assess the nutritive value of wheat in terms of amino acids. Considerable space is given to the relative failure of wheat protein to meet the nutritional needs of young rats, owing to insufficiency of lysine, but no evidence is presented which bears on the suitability of the amino acid mixture in wheat for human nutrition. The preparation of high protein flours from soft wheats by "air-classification" of the particles of flour is discussed. In this way it is possible to obtain a flour with 3 times the protein content of the original.

In the section on lipids, the content of polyunsaturated fatty acids is discussed in relation to the possible role of deficiency of these acids in causing arterial disease, but no definite conclusions are drawn. In fact, the data on the quantities of these acids in wheat preparations still appear to be limited.

The review ends with a brief account of agene and chlorine dioxide.

[After the victory of the millers in 1955 there appears to be a temporary lull in the campaign for better and more nutritious "national flour". When the fighting is resumed, this review will be essential reading for all requiring scientific evidence on the subject.]

*R. Passmore*

Leali, L. Ricerche sulla colimetria del latte. [***Escherichia coli* Detection in Milk**] *Igiene Moderna.* 1958, Sept.–Oct., v. 51, Nos. 9/10, 665–718, 1 coloured pl. [Numerous refs.] English summary.

An extensive investigation of specimens of milk naturally and artificially contaminated with *Escherichia coli* and other bacteria has been carried out with many of the media often used for this purpose, *i.e.* 13 in all. Both solid and fluid media have been investigated and paper strips which have been soaked in media.

The main conclusion is that although the results are approximately equivalent with several of these, the broth containing 0·2% of the chloride of triphenyl tetrazolium is the best of all the media investigated for the detection of *E. coli* on account of simplicity, speed and cheapness. The medium was prepared by making a stock solution of 2% tetrazolium, with the powdered preparation marketed by the German firm Heyl under the name of "Rubrognost", and diluting this stock solution in unneutralized broth *p*H 6·2–6·4. On this media milks containing *E. coli* alone or in mixture with other bacteria produce a deep red brown colour within 12 hours. *Salmonella* and *Aerogenes* strains do the same but more slowly especially when small inocula are used. None of the other bacteria tested produce this colour; *Proteus*, *Pseudomonas* and *Brucella* strains produce a light rose colour. *J. W. McLeod*

Ministère De La Santé Publique. Paris. De la destruction des bactéries par la chaleur. Étude de l'efficacité de la pasteurisation du lait. [**Destruction of Bacteria by Heat: Study of the Efficacy of Pasteurization of Milk**] [Nevot, A., Lafont, P. & Lafont, J., with the technical collaboration of M. Henry & L. Derouet]. *Monographie de l'Institut National d'Hygiene No. 18.* 139 pp., 75 graphs & 3 figs. [50 refs.] 1958. Paris (16e): Inst. Nat. Hyg., 3, rue Léon-Bonnat.

The *Conseil Superieur d'Hygiene publique de France* (1955) recommended that 63°C. for 30 minutes be used for the "low" and instantaneous heating at 95°C. for the "high" pasteurization of milk. Furthermore, that as this treatment would not ensure sterility nor destruction of the tubercle bacillus both raw and pasteurized milk should be boiled for 5 minutes at least. In the discussion the authors quoted the method of pasteurization used in other countries namely 62°C. for 30 minutes and 72°C. for 16 seconds (High Temperature Short Time—HTST). Their comments were disregarded and as a result they undertook the research project described in this monograph.

The work was divided into 2 parts, the laboratory determination of the thermo-resistance of pathogenic bacteria which could be present in milk and of other organisms commonly found in milk, and the efficiency of pasteurization times and temperatures with a facsimile model of the plant common in modern industrial installations.

Experiments were carried out with (a) bacteria responsible for animal diseases, *e.g. Brucella*, bovine and avian tubercle bacilli, $\beta$-haemolytic staphylococci and species of streptococci from groups B and C of Lancefield; (b) organisms carried by normal animals, *e.g.* salmonellae and bacterial agents of toxic substances and (c) pathogenic bacteria excreted by human cases or symptomless excretors which may be transmitted by intermediate agencies such as wash water or milk vessels, *e.g.* staphylococci, streptococci, salmonellae, shigellae, cholera vibrios, *Escherichia coli* of the serological types causing infantile enteritis, diphtheria bacilli and tubercle bacilli.

The results are fully illustrated with many graphs and tables which are clearly presented and provide ample evidence for the efficiency of well-established practices regarding times and temperatures of pasteurization.

The results indicated primarily that of the species of bacteria pathogenic for the cow, and thus presenting a particular hazard to the consumer, the brucellae are more heat-resistant than tubercle bacilli, and the salmonellae were more sensitive than both the preceding species.

Of the organisms which sour milk and jeopardize the keeping quality, enterococci were the most difficult to destroy; in decreasing order of heat-resistance were *Klebsiella aerogenes*, *Proteus*, staphylococci and coliform bacilli and the paracolon bacilli of the *aerogenes* type, *Pseudomonas pyocyanea*, the paracolon bacillus of the *anaerogenes* type and neighbouring species, and certain bacteria of the flora of Veillon. The following pathogenic bacteria were more easily destroyed by heat than the brucellae, certain $\beta$-haemolytic streptococci, diphtheria bacilli and coliform bacilli of the serological types O11B4, O55B5, O26B6; Lancefield group C streptococci were more heat-resistant than the brucellae.

Strains of bacteria tested from a single species varied little in their reaction to heat but it seemed that the lethal effect was not shown by all individuals simultaneously so that small variations in sensitivity may be a function of density; variations in *p*H may cause slight differences also.

It is stated that after heating milk to temperatures which ensure the destruction of all bacteria, phosphatase activity still exists in the milk.

The results obtained indicated that the HTST pasteurization, *i.e.* the holding of milk for 10 seconds at 72°C., ensured the destruction of all pathogenic bacteria able to contaminate milk. Of the common milk organisms enterococci only will be left. To augment the margin of safety a temperature of 72°C. for a time longer than recommended for phosphatase inactivation may be used.

To advocate pasteurization other than 62°C. for 30 minutes or 72°C. for 10–20 seconds gives no advantage hygienically; those saprophytic species of bacteria which are able to survive can in fact survive much higher temperatures.

The authors conclude by saying that not to recognize in such methods of pasteurization their prophylactic value against bacterial infection transmissible by milk, is to neglect the opinion of authors who for several decades have demonstrated their efficiency. This opinion summarized by G. S. WILSON in the words " . . . if pasteurization was rendered compulsory and universal, milk-borne disease would practically cease to exist . . ." [this *Bulletin*, 1942, v. 17, 740] is endorsed by the authors. *Betty C. Hobbs*

# Bacteriology and Immunity

*Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the* TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-division of this section*

## GENERAL

MINISTRY OF HEALTH. CENTRAL HEALTH SERVICES COUNCIL. Standing Medical Advisory Committee. **Staphylococcal Infections in Hospitals.** Report of the Sub-Committee [COHEN OF BIRKENHEAD, Chairman]. pp. iii + 36 pp., 1 fig. [29 refs.] 1959. London: H.M. Stationery Office. [2s. 6d.]

This memorandum defines the problem of staphylococcal cross-infection in hospitals, and details the measures necessary for preventing it. Most of these are familiar to those acquainted with the problem, but not all of them are possible in many hospitals, and the importance of this publication seems to be that it will justify demands on Hospital Boards for further staff and equipment and even structural changes.

For the "ascertainment" of infection it is recommended that the Sister of each ward should keep a register in which particulars of each case are noted. There should be some means of ascertaining infection developing after discharge from hospital: post-puerperal mastitis is cited as a common instance of this. Each hospital should have a Control of Infection Committee, to one member of which, the Control of Infection Officer, executive functions are delegated. The importance of bacteriological examinations is stressed: cultures of staphylococci should be kept, and when an outbreak of infection occurs, phage typing is necessary to determine its mode of spread.

The isolation of infected cases is essential, and 20% is mentioned as the proportion of beds which should be in single rooms. [This and the recommendation that all dressings should be done in a specially ventilated treatment room, are perhaps the least generally feasible proposals made.] It is emphasized that strict asepsis, and not antibiotics, should be relied on for the prevention of infection, and rules are given for a variety of aseptic procedures, including definition of the circumstances in which gowns and masks or gloves should be worn, methods of disposal of contaminated material, the protection of sterile materials against contamination, the disinfection of bedding, washing facilities etc. 3 appendices are devoted to Rules for Isolation Nursing, Rules for the Performance of Wound Dressings, and Operating Theatre Practices. A preceding chapter defines the duties in connexion with this subject of different members of the hospital staff, nursing, medical and lay, and of the Hospital Management Committee. It is acknowledged that in order to carry out all the detailed recommendations made, extra staff and more generous supplies of sterile materials may be necessary. *L. P. Garrod*

BRINTON, C. C., Jr. **Non-Flagellar Appendages of Bacteria.** *Nature.* 1959, Mar. 21, v. 183, 782–6, 8 figs. [17 refs.]

The recently discovered filiform appendages found growing from the surface of many different species of bacteria are visible only by electron microscopy and the first clear description of these appendages, as seen under the electron microscope, was given by HOUWINK and VAN ITERSON, (*Biochim. et Biophys. Acta*, 1950, v. 5, 10). [Nevertheless it seems possible that the observations of TOPLEY and AYRTON (*J. Hygiene*, 1924, v. 23, 198) on, what they called the "X antigen", were related to these pili, bristles, fimbriae or filaments, as they are variously called.] A number of immunological studies by DUGUID and his colleagues [this *Bulletin*, 1956, v. 31, 861; *ibid.*, 1958, v. 33, 264; *J. Path. Bact.*, 1958, v. 75, 519] have been concerned with haemagglutination and agglutination activities related to these bacterial fimbriae.

The present author, who prefers to call the appendages "pili", has been working on the subject for several years and in this article he summarizes the results of his, and his colleagues' investigations on the genetics, biological activity, chemistry and electrophoresis of bacterial pili. The paper is of considerable interest but, because of its condensed nature, is hardly suitable for further summarization.

*H. J. Bensted*

Tortori-Donati, B. Importanza delle forme L in patologia umana. [**Importance of L Forms in Human Pathology**] *Igiene Moderna.* 1958, Nov.–Dec., v. 51, Nos. 11/12, 903–27. [103 refs.] English summary (9 lines).

Rappaport, F., Rabinovitz, M. & Konforti, N. **An Improved Method for the Preparation of Sulphur and Iron containing Differentiation Media.** *Applied Microbiol.* Baltimore. 1958, July, v. 6, No. 4, 264–5, 1 fig.

A modification of the medium previously described [this *Bulletin*, 1956, v. 31, 741] for the demonstration of urease, acid and gas production from mannitol, indole and H$_2$S production is as follows:

| | |
|---|---|
| Tryptone … … … … | 15·0 gm. |
| NaCl … … … … … | 5·0 gm. |
| Ferric ammonium citrate … … | 0·1 gm. |
| Mannitol … … … … | 1·5 gm. |
| Na$_2$CO$_3$ (anhydrous) … … … | 0·7 gm. |
| Tryptophan … … … … | 0·4 gm. |
| Phenol Red … … … … | 0·025 gm. |
| Agar … … … … … | 20·0 gm. |

The ingredients are thoroughly mixed into a stock dry powder which keeps well. 4·27 gm. of this is dissolved in 100 ml. distilled water, heated to boiling then distributed in tubes in 2·5–3·0 ml. volumes without *p*H adjustment and autoclaved. For use, the tubes are remelted, one drop (0·03 ml.) of urea-thiosulphate solution is added and they are slanted to set. The urea-thiosulphate solution consists of Na$_2$S$_2$O$_3$ 15 gm. dissolved in 100 ml. of urea solution (urea 50 gm., water 100 ml.). This solution is self-sterilizing in 24 hours and is stable. When it does deteriorate it becomes turbid.

This improved medium combines the advantages of the earlier one without the disadvantage of deterioration of sulphur compounds during storage and autoclaving. In consequence it is very suitable for the detection of slow producers of H$_2$S.

Substitution of 1·0 gm. sorbitol for the mannitol gives a sorbitol-iron-agar which may be used to distinguish pathogenic *Escherichia coli* strains which ferment sorbitol from the non-pathogenic ones which do not.

*J. Nagington*

Wertman, K. & Groh, Margaret. **The Effects of Thiamine Deficiency on Some Physiologic Factors, Phagocytosis and Susceptibility to Infection.** *J. Immunology.* 1959, Mar., v. 82, No. 3, 241–7. [10 refs.]

"Male white rats of the Sprague-Dawley strain were maintained on a well-defined diet deficient in thiamine, and a) various physiologic factors of importance to infection, b) phagocytosis and c) susceptibility to infection were studied. Adequate numbers of inanition and *ad libitum* control animals were included. The following physiologic factors were studied: a) the cellular composition of the peripheral blood, b) complement activity, c) cellular migration in inflammation, d) the cellular composition of the exudate in inflammation and e) 'leukotaxine' activity.

"The following observations were made from these studies:

"1. No change was noted in the total leucocyte count in the peripheral blood. An increase in erythrocytes and hemoglobin concentration was evident in the thiamine deficient and inanition controls. Differential cell counts of the blood leucocytes of the vitamin deficient and inanition controls showed an absolute and relative increase in polymorphonuclear cells and a reduction in the percentage of lymphocytes.

"2. Complement activity of the sera of the thiamine deficient rats was less than either the inanition or *ad libitum* control rats.

"3. There was a marked decrease (50%) in the total number of leucocytes in the peritoneal exudates of the thiamine deficient animals when inflammation was established.

"4. A relative granulocytosis with an absolute decrease was observed in the exudates removed from the inflamed areas of the deficient animals as compared with the controls.

"5. No alteration in capillary permeability, as measured by the Menkin dye accumulation technique, was noted in any group.

"6. Thiamine deficiency had no apparent effect on the capacity of the leucocyte to phagocytize *Diplococcus pneumoniae.* Phagocytosis was approximately the same in all groups of animals.

"7. Thiamine deficient animals were highly susceptible to *D. pneumoniae.* However, after receiving 40 $\mu$g of thiamine daily for seven days, they were able to resist the invasion and infection.

"8. The reduced complement activity and cellular migration to the site of inflammation suggest that these significant factors play a role in the inability of a thiamine deficient animal to resist bacterial infection."

Schaechter, M., Bentzon, M. W. & Maaloe, O. **Synthesis of Deoxyribonucleic Acid during the Division Cycle of Bacteria.** [Correspondence.] *Nature.* 1959, Apr. 25, v. 183, 1207–8.

Swartz, M. N. & Gordon, Nancy. **Agarase from an Agar-Digesting Bacterium.** *J. Bacteriology.* 1959, Apr., v. 77, No. 4, 403–9, 4 figs. [26 refs.]

McCarthy, B. J. **Variations in Dehydrogenase and Deaminase Activity during Bacterial Growth.** *Proc. Roy. Soc.* Ser. B. 1959, Apr. 21, v. 150, No. 940, 410–22, 6 figs. [17 refs.]

Lubin, M. **Selection of Auxotrophic Bacterial Mutants by Tritium-Labeled Thymidine.** *Science.* 1959, Mar. 27, v. 129, 838–9. [10 refs.]

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## BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

*In this section the abstracts are arranged as far as possible in the following order:—General; Antibiotics; Other Therapeutic Substances; Disinfection.*

Schneierson, S. S. & Amsterdam, D. **A Simplified Tube Procedure for the Routine Determination of Bacterial Sensitivity to Antibiotics.** *Amer. J. Clin. Path.* 1959, Jan., v. 31, No. 1, 81–6, 2 figs.

Small volumes of antibiotic solutions are placed in tubes and kept frozen. When a test is to be carried out, the required volume of broth, already inoculated with the organism, is added. The advantages of this method are that large numbers of the tubes can be kept available, and the ease of actual performance, reliability and cheapness. Each individual test consists of 3 tubes, a growth control, and 2 containing final concentrations of antibiotic corresponding to those obtainable in the blood by ordinary and high doses. [In the Table of information about these concentrations, misalignment seems to have produced confusion: no values are given for 7 of the antibiotics named in the Table, including erythromycin, tetracycline and streptomycin.] *L. P. Garrod*

Lindenmann, J. Theorie und Praxis der Resistenzbestimmung. [**Theory and Practice of Sensitivity Tests**] *Schweiz. med. Woch.* 1958, Dec. 27, v. 88, No. 52, 1315–18, 4 figs. [10 refs.]

This paper from the Institute of Hygiene of the University of Zürich is a judicial appreciation of the indications for and the interpretation of tests of bacterial sensitivity to antibiotics and sulphonamides. The organism tested must be known to be the cause of the infection, and the culture used must be representative of the bacterial population in the body: a remarkable diagram of a pair of lungs is reproduced showing how the drug resistance of tubercle bacilli can vary in different areas. Tube dilution tests are advisable for this organism, but for staphylococci, the other species for which sensitivity tests are most necessary, the diffusion test with disks is considered satisfactory. When sensitivity is invariable, as in pneumococci and haemolytic streptococci to penicillin, no test is necessary. The results of tests of *Salmonella*, *Shigella*, *Proteus* and *Pseudomonas* are described as " notoriously misleading " [adequate reasons for this view are not given: the mere fact that streptomycin is ineffective in enteric fever despite the sensitivity to it of the causative organism, does not seem to justify so sweeping a condemnation]. The significance of tests with sulphonamides is said to lack precision, and there is no simple and satisfactory way of testing the action of combinations. Penicillin is to be preferred to other antibiotics when the organism is sensitive to it. *L. P. Garrod*

Goodier, T. E. W. & Parry, W. R. **Sensitivity of Clinically Important Bacteria to Six Common Antibacterial Substances.** *Lancet.* 1959, Feb. 14, 356–7.

During the years 1956–7 all strains of supposedly pathogenic bacteria isolated from clinical material in a general hospital near London were tested for sensitivity to penicillin, streptomycin, chloramphenicol, tetracycline, erythromycin and a sulphonamide by streaking on a plate at right-angles to a blotting paper strip soaked in a solution of the drug. The frequency of sensitivity to each drug is stated according to the species of organism, the site of the infection, and whether derived from an in- or an out-patient. A much greater frequency of resistance in strains from in-patients, and applying only to penicillin, streptomycin and sulphonamide, was found only in staphylococci, and this increased somewhat during the period of study. Particulars are given of the quantities of each antibiotic used in the hospital in 1 year, and the descending order of these quantities is the same as the diminishing order of frequency of bacterial resistance. *L. P. Garrod*

Lázár, J. **Contributions to the Problem of Antibiotic-Antagonism.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 4, 337–42, 4 figs. [12 refs.]

This author, from Debrecen, Hungary, has studied combined antibiotic action by the method in which blotting paper strips containing different antibiotics are placed on an inoculated plate of medium at right-angles, the nature of their combined action being judged by the contour of the edge of the inhibition zone in the angle between them. These appearances are illustrated, but [perhaps owing to poor reproduction] not altogether convincingly. The organisms used were multiple strains of *Staphylococcus aureus* and *Escherichia coli* and 1 each of a few other species: the drugs were penicillin, chloramphenicol, streptomycin, chlor- and oxytetracycline and a sulphonamide. Whether antagonism, synergy or merely a " neutral " effect was produced by various combinations of these against each organism is clearly shown in a Table. The most notable feature of this is the frequent occurrence of antagonism between streptomycin and chloramphenicol or either tetracycline against staphylococci. Penicillin in such combinations rarely had such an effect, and combinations of chloramphenicol, tetracyclines and sulphonamide often showed synergy. [The validity of this simple method is questionable. 12 out of a total of 30 organisms were acted on synergically by the combination of chlor- and oxytetracycline, 2 such closely related antibiotics that synergy between them is very difficult to imagine or explain.] *L. P. Garrod*

OSKAM, H. J. & KOELMAN, A. Recherches sur l'antagonisme d'une part, et le renforcement d'activité d'autre part de quelques antibiotiques combinés par paires. **[Studies on Antagonism and Potentiation of Some Antibiotics associated by Pairs]** *Ann. Inst. Pasteur.* 1959, Mar., v. 96, No. 3, 372–5, 2 figs.

These authors from Utrecht have devised a method, for the description of which the reader is referred to a paper in press, of calculating an "index of interference" between 2 antibiotics. This is based on estimations of turbidity made after 2½, 5, 7½ and 24 hours of cultures of *Staphylococcus aureus* containing each antibiotic or both [evidently in sub-inhibitory concentrations, but how these are chosen is a vital piece of missing information]. One of two graphs illustrating such results shows that there may be decided differences up to 7½ but none at 24 hours [*i.e.* growth is delayed, but apparently compensates for this by increased subsequent rate: can it safely be concluded that a combination having such an effect exhibits "potentiation" in any therapeutically useful sense?]. By such means it was shown that the combination of tetracycline with erythromycin, spiramycin or oleandomycin exhibits potentiation (index of interference = >1·0) whereas each of the 3 possible combinations of the 3 last-named exhibits antagonism.

*L. P. Garrod*

ZWART VOORSPUIJ, A. J. & BOKMA, L. H. **The Simultaneous Action of Two or More Antibacterial Agents. The Action of the Combination Nitrofurantoin - Chloramphenicol - Erythromycin on** *Proteus vulgaris. Antibiotics & Chemotherapy.* New York. 1959, Jan., v. 9, No. 1, 27–37, 8 figs.

This paper is based on only 2 experiments, in each of which the minimum inhibitory concentration for *Proteus vulgaris* of mixtures of drugs was determined. In the first nitrofurantoin and chloramphenicol were mixed in 9 different relative proportions as well as being tested alone: the results of this are presented in a single line graph of conventional form [Fig. 3, a second graph, presenting them in different terms, is printed upside down]. In a second experiment nitrofurantoin, chloramphenicol and erythromycin were mixed in 41 different relative proportions and the minimum inhibitory concentrations of these mixtures were determined. The results are stated in a table, but they are also presented graphically in different terms in 5 graphs of triangular shape. The table includes a mathematical expression of the degree of synergy or antagonism observed, values for the concentration of each mixture attainable therapeutically in the urine, and for an "activity quotient" calculated from this (*e.g.*, the highest activity quotient, 18·7, is given by a mixture of 45 parts each of nitrofurantoin and erythromycin and 10 of chloramphenicol, the minimum inhibitory concentration being 17·8 μgm./ml. and that attainable in the urine 333·3 μgm./ml.). The authors believe that "standardization of terms and methods in this field is overdue". [While admiring their industry, other workers may be reluctant to adopt such elaborate methods, particularly since it has yet to be proved that effects predicted on this basis will actually be obtained therapeutically. The choice of the antibiotics used is not explained: both are less active against this species than, for instance, novobiocin or (usually) streptomycin.]

*L. P. Garrod*

ZABŁOCKI, B., ROLICKA, M. & SZYDŁOWSKI, S. **Inactivating Properties of Antibodies against Antibiotics** *in vitro. Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1958, v. 6, Nos. 11/12, 475–81, 2 figs. [18 refs.]

This work is pursuant to that of LOISELEUR [this *Bulletin*, 1952, v. 27, 294], who found a peculiar type of antibody in the serum of animals treated with penicillin: such serum underwent an increase in viscosity on the addition of penicillin. The present authors gave rabbits intramuscular injections of penicillin 3 times a day for 15–17 days and bled them 3 days later. The serum, when mixed with a solution of penicillin, underwent an increase in viscosity: this was maximal (an increase of not more than 12% over normal) in the presence of 1 mgm. of penicillin per ml. of serum. Such "immune" sera were tested for "anti-penicillin" activity: how this was done is not sufficiently explained, but it seems that in tests with 2 strains of staphylococci the activity of penicillin against them was unaffected, whereas with 2 others which had been "subjected to the action of nucleic acid isolated from a sensitive strain" it was reduced. During storage of these sera, anti-antibiotic activity was lost more rapidly than their capacity to develop increased viscosity. They gave no precipitin reaction with penicillin, nor did they agglutinate penicillin-treated red cells. Sera of rabbits immunized with streptomycin or oxy- or chlortetracycline gave the increased viscosity reaction to a lesser degree but had no anti-antibiotic activity.

*L. P. Garrod*

WEISS, W., NADEL, J., EISENBERG, G. M. & FLIPPIN, H. F. **Oral Penicillin G and Penicillin V.** *Amer. J. Med. Sci.* 1959, Feb., v. 237, No. 2, 205–11, 1 fig. [47 refs.]

This paper disputes the alleged superiority of penicillin V over penicillin G administered orally. The only new observation described was the treatment of 51 cases of acute streptococcal sore throat, 25 with G and 26 with V, in equal doses. By 3 criteria the effects were indistinguishable: hence it is argued that G is so good that V could "do no more and might even do less". It is maintained that no controlled clinical observations indicate any advantages of V over G. Although it is granted that V may produce higher blood levels than G, some investigators are said to have questioned this. It is pointed out that some organisms are more susceptible to G than to V [but not that the converse is true of others]. Observations are also cited suggesting that V suffers more than G from protein binding and inactivation in the tissues. [This is a highly tendentious paper, selecting from the literature such few observations as support the authors' thesis. The fact remains that, dose for dose, about twice as much V as G is excreted in the urine and must therefore have been available for therapeutic action. If a corresponding difference in clinically observable effect has never been proved, this may well be because a controlled trial adequate to establish such a difference would be a very formidable undertaking.] *L. P. Garrod*

LUTZ, A. Donnèes expérimentales sur la phényracilline et son association avec la dihydrostreptomycine. **[Experimental Data on Phenyracillin and its Association with Dihydrostreptomycin]** *Ann. Inst. Pasteur.* 1959, Mar., v. 96, No. 3, 260–67, 2 figs.

Phenyracillin is the dipenicillinate of 2,5-diphenylpiperazine. A single dose of 300,000 units of this, sodium penicillin and benzathine penicillin was given to dogs and the antibiotic was assayed in the blood at intervals. Sodium penicillin produced high early levels, but disappeared after the 8th hour. The concentrations produced by phenyracillin were intermediate and those of benzathine penicillin the lowest, these two curves converging at 24 hours: the few observations made after this time suggest that benzathine penicillin was persisting longer. In a further series of experiments 300,000 units of phenyracillin, 300 mgm. of dihydrostreptomycin or both were given to dogs and the bactericidal power of their serum was determined at intervals up to 10 hours, the serum alone or diluted with an equal volume of broth being inoculated with staphylococci and submitted to viable counts after 14, 36, 60 and sometimes 84 and 108 hours. The combination had a strong or complete bactericidal effect, even up to the 10th hour, when sera containing only 1 antibiotic had less or no activity. Phenyracillin was well tolerated. [The solubility of this new form of penicillin is not mentioned: presumably it is low, and like benzathine penicillin, it must have been administered as a suspension.] *L. P. Garrod*

OLITZKI, A. L. & GODINGER, Dinah. **Investigation on Streptomycin Inhibitors with the Aid of a Streptomycin-Dependent** *Vibrio comma. J. General Microbiol.* 1959, Feb., v. 20, No. 1, 54–60, 1 fig. & 1 pl.

*Pseudomonas pyocyanea* having been said to produce a "streptomycinase", LIGHTBOWN [this *Bulletin*, 1955, v. 30, 345] extracted cultures of this organism and obtained a substance which antagonized streptomycin: some other species examined did not form it. The present authors have prepared extracts of a large variety of bacteria and tested them by addition to streptomycin solution, incubation for 3 hours, and placing the mixture in glass cylinders on the surface of plates of medium containing starch and pre-seeded with a streptomycin-dependent *Vibrio comma*. After incubation these were flooded with a solution of iodine. Antagonistic action was then indicated by a diminution in size of the zone around the cylinder in which growth could occur and the starch was decomposed. Extracts of *Ps. pyocyanea* had the most pronounced antagonistic effect, but some was also exerted by extracts of *Proteus morgani*, 2 species of *Bacillus* and 4 of *Clostridium*. No effect was obtained with 6 other species of Gram-negative rod, 4 of Gram-positive cocci and 2 yeasts. *L. P. Garrod*

EISENBERG, G. M., WEISS, W. & FLIPPIN, H. F. **The Effect of Ethylenediaminetetraacetic Acid (EDTA) and Ascorbic Acid on Tetracycline Blood Serum Concentrations.** *J. Lab. & Clin. Med.* 1958, Dec., v. 52, No. 6, 895–8.

Only 6 normal subjects were used in a study of the absorption of tetracycline, and only a single specimen of blood was examined after the dose had been given, the interval being 3 hours. The dose of tetracycline was 250 mgm. and 2 other substances were given with it. Ethylenediaminetetraacetic acid [EDTA] was chosen because it is a powerful chelating agent, and was expected to act like citric acid in sequestering calcium [this *Bulletin*, 1958, v. 33, 380 *bis*]. Instead of increasing absorption of the antibiotic it had the opposite effect: this was the only significant difference among all the results, and the authors do not explain it. Ascorbic acid has been said by some authors to enhance absorption: this was not confirmed. [If either of these substances had caused either very rapid absorption, or enhanced but delayed absorption, this over-simplified method of test would not necessarily have revealed it.] *L. P. Garrod*

SENSI, P. & TIMBAL, M. T. **Isolation of Two Antibiotics of the Grisein and Albomycin Group.** *Antibiotics & Chemotherapy.* New York. 1959, Mar., v. 9, No. 3, 160–66, 1 fig.

"From the fermentation liquors of two different *Streptomyces* strains, two antibiotics (L.A. 5352 and L.A. 5937) belonging to the grisein-albomycin group were isolated. They showed cross resistance mutually as well as with albomycin. L.A. 5352 contains loosely bound iron, while L.A. 5937 does not contain iron. The similarities and differences with the known antibiotics are discussed. An investigation was made on the frequency of resistant mutants in a culture of *Micrococcus aureus* used as test organism. The activity spectra, based on the inhibition zones on plate, and toxicity data are reported. The two antibiotics show in vivo activity, but the high percentage of spontaneously resistant bacteria limits their therapeutic usefulness."

MORDARSKI, Marian, WIECZOREK, Jadwiga & KRZYWY, T. **WR 3/17, a New Antibiotic. I. Discovery and Biological Studies.** *Antibiotics & Chemotherapy.* New York. 1959, Feb., v. 9, No. 2, 90–96, 2 figs.

This new antibiotic was obtained from an organism "in the *Streptomyces albus* group" but differing from others hitherto described: it was isolated in the course of an extensive survey of Polish soils carried out at Wroclaw. The cultural characters of the organism are described, and the conditions in which the antibiotic is produced: interesting features are the necessity for an inorganic source of nitrogen, and rapid loss of activity in the fermentation liquor after 2 days' incubation, accompanied by mycelial autolysis. The antibiotic exhibits maximum potency at *p*H 8·0, having only one-tenth of this activity at *p*H 6·0; on the other hand, its high thermolability is greater at *p*H 8·0 than at *p*H

5·0. Its minimum inhibitory concentration for staphylococci is 0·15 or 0·3 $\mu$gm./ml. and several other Gram-positive cocci tested (not including *Streptococcus pyogenes*) were also highly susceptible, as, to a slightly lesser degree, were tubercle bacilli and 3 species of *Bacillus*. Most Gram-negative organisms tested were much more, but not totally, resistant; and exception was *Brucella suis*. A remarkable finding is that 3 strains of *Candida albicans* were inhibited by 25 $\mu$gm./ml. Staphylococci and *Str. faecalis* abnormally resistant to 6 of the major antibiotics were normally sensitive to it. No toxic effects were seen in mice given repeated doses of as much as 50 mgm./kgm. by injection. An account of the chemical and physical properties of WR 3/17 is promised in a further paper. No trial in experimental infections is mentioned.

*L. P. Garrod*

CIAK, Jennie & HAHN, F. E. **Mechanisms of Action of Antibiotics. II. Studies on the Modes of Action of Cycloserine and its L-Stereoisomer.** *Antibiotics & Chemotherapy*. New York. 1959, Jan., v. 9, No. 1, 47–54, 5 figs. [22 refs.]

Natural cycloserine is D-4-amino-3-isoxazolidone: these authors have compared its behaviour with that of the synthetic L-isomer. Their minimum inhibitory concentrations differ: 2 strains of *Escherichia coli* were of approximately equal sensitivity to both isomers [the data for one of these strains in Table 1 do not quite tally with those shown graphically in Figs. 2 and 3] but *Salmonella typhi*, *Bacillus subtilis*, *Staphylococcus aureus* and *Streptococcus pyogenes* were all much more sensitive to the D-isomer. This substance acting on *E. coli* in a nutritive medium produces lysis, against which the organism can be protected by the presence of sucrose. The L-isomer inhibits growth without causing any lysis. The D-isomer acts like penicillin in causing the accumulation of N-acylamino sugar in *Staph. aureus*, an effect attributable to interference with cell wall synthesis. It thus appears that the D-isomer may have an action like that of penicillin on the cell wall. The action of the L-isomer is evidently different, and it appears to follow from this that substances of closely similar chemical structure can act in quite different ways.

*L. P. Garrod*

THOMPSON, R. E. M. & O'GRADY, F. **Rapid Screening of Antifungal Agents for *in vivo* Activity.** *J. Path. & Bact.* 1959, Jan., v. 77, No. 1, 302–6, 3 figs.

Mice were inoculated intramuscularly in the left thigh with *Candida albicans* suspension, and treated by daily subcutaneous injections of drugs at another site, the diameter of the inoculated limb being measured daily. In untreated animals the swelling produced reached a peak on the 2nd day and a second on about the 5th. A significant reduction in this inflammatory response was produced only by pentamidine and mycostatin (nystatin); sodium iodide, stilbamidine, hydroxystilbamidine, sulphathiazole and sodium sulphadimidine had no effect.

*L. P. Garrod*

HIGO, N. **Studies on Antiviral Antibiotics produced by *Streptomyces*. XI. Effect of Phagostin on the Multiplication of Bacteriophage T3.** *Japanese J. Microbiol.* 1958, July, v. 2, No. 3, 203–15, 8 figs. [18 refs.]

Phagostin, the properties of which were described in a previous paper (*J. Antibiotics*, Ser. A., 1957, v. 10, 74), is a product of a search for antiviral antibiotics. This substance has been found to inhibit the growth of bacteriophage T3 in a concentration of 1 $\mu$gm./ml. At this concentration it did not prevent the growth of the host cell, *Escherichia coli*, strain B: it did not inactivate free phage, nor did it prevent the intracellular multiplication of phage: it appeared to act by preventing the lysis of infected cells. Such cells were also resistant to lysis by cyanide, but could be lysed by ultrasonic vibration with the liberation of active phage.

*L. P. Garrod*

GERBER, P., DUTCHER, J. D., ADAMS, E. V. & SHERMAN, J. H. **Protective Effect of Seaweed Extracts for Chicken Embryos infected with Influenza B or Mumps Virus.** *Proc. Soc. Exper. Biol. & Med.* 1958, Dec., v. 99, No. 3, 590–93, 2 figs. [13 refs.]

Some tests for antiviral activity in the chick embryo gave erratic results when the insoluble compound under test was introduced as a suspension in 0·25% agar. This led to an examination of agar itself, and experiments were done with polysaccharides from *Gelidium cartilagenium* (the usual source of agar) and with carrageenan, a galactan from *Chondrus crispus*. Each of these substances, when injected into the allantoic cavity in a dose without effect on the embryo (*e.g.* 1·25 mgm.) protected 70% more of the embryos against mumps or influenza B virus introduced by the same route. It had no effect on influenza A or Newcastle disease virus. An inert suspending medium, such as carboxymethyl cellulose, must therefore be used in experiments with the 2 former viruses.

*L. P. Garrod*

CAWSON, R. A. & CURSON, I. **The Effectiveness of Some Antiseptics on the Oral Mucous Membrane.** *Brit. Dental J.* 1959, Mar. 17, v. 106, No. 6, 208–11.

An area of buccal mucosa anterior to Stenson's duct was swabbed; an antiseptic was then applied to it and it was swabbed again 15–30 seconds later, both swabs being cultivated on blood agar and the second also in a tube of meat broth. Growths from the second were classed as "heavy", "medium", "light" and "nil". Some treatments produced at least a few of each of these kinds of culture (*i.e.* the results were not consistent), but a high proportion of sterile cultures with no heavy growths was given only by iodine (2·5% tincture or 2% watery solution) and Hibitane (chlorhexidine, in 2% alcoholic solution): after treatment with these antiseptics, about 50% of cultures were sterile even in meat broth. Some tests were made which satisfied the authors that carry-over of antiseptic was not inhibiting growth. Unsatisfactory results were given by 70 and 90% alcohol, 2% Dettol, (= 1·44% *p*-chlor-*m*-xylenol), 2% Roccal, and tincture of metaphen (0·33% metaphen).

The object of these experiments was to decide whether disinfection of the surface is feasible before injection of a local anaesthetic. *L. P. Garrod*

ADAMS, R., FAHLMAN, B., DUBE, Edna W., DUBE, F. J. C. & READ, S. **Control of Infections within Hospitals. Special reference to Prevention with Operating Rooms.** *J. Amer. Med. Ass.* 1959, Apr. 4, v. 169, No. 14, 1557–67, 6 figs.

This paper from the Huggins Hospital, Boston University School of Medicine, describes an investigation prompted by the occurrence of infection in clean operation wounds, and recommends various measures for preventing such infections. The first conclusion reached is that ordinary domestic cleaning of patients' rooms and wards is inadequate: satisfactory freedom from bacteria was only attained when a conscientious workman cleaned the walls, floor, ceiling and "every item in the room" daily with Tergisyl (this contains sodium xylene sulphonate, triethanolamine dodecyl benzene sulphonate, *o*-phenylphenol and *p*-tertiary amylphenol). Blankets were sterilized by adding 2% Amphyl (*o*-phenylphenol and *p*-tertiary amylphenol) to the final laundry rinse. Operating theatre conditions are discussed at length, from the point of view of cleaning, ventilation (positive pressure filtered air) and the erection of a barrier, at which there is an antiseptic-soaked blanket on the floor, beyond which no contaminated blanket, cart (trolley) or ordinary outer clothing or shoes are allowed to pass. A new type of closely fitting mask has been devised which is said to be highly efficient [this is illustrated, but the material of which the filter is composed is not specified]. After 18 other trials, a "sexless, sizeless, sideless quick-change double-breasted" gown has been adopted, and feet are inserted into a "washable, flexible, slip-on, wrap-around, cloth-top conductive rubber-soled bootie". An important further precaution is to seal off the patient's skin in the operative area by covering it with an adherent plastic film. [This paper contains much doubtless admirable advice, but the results of the investigations on which it is based are stated in only general terms. There is little about bacteriological methods: when numbers of bacteria obtained with a "sieve sampler" are mentioned the volume of air they represent is not stated, and nothing is said anywhere about whether bacteria cultivated included any pathogenic species. The authors do not say how long these methods have been in use, and how many infections, if any, have occurred since their adoption.] *L. P. Garrod*

HUDSON, P. B., SANGER, G. & SPROUL, Edith E. **Effective System of Bactericidal Conditioning for Hospitals.** *J. Amer. Med. Ass.* 1959, Apr. 4, v. 169, No. 14, 1549–56, 9 figs.

This paper is from the Francis Delafield Hospital, a "300-bed general cancer hospital" staffed by Columbia University and administered by the City of New York. It describes some effects of using 4 disinfectant solutions for various purposes. The composition of these is stated: they contain from 4 to 9 ingredients each, and are intended for application to floors, walls and other surfaces, air-filters, mattresses, laundry, furniture, etc. The effect of their use was judged by bacterial air counts: these were carried out simply by exposing culture plates for 1 hour. When all 4 disinfectants were being used the counts obtained fell considerably. One application made was to air filters both supplying air to the wards and re-circulating it within them: this was stopped while other uses were continued, and the rise in count which followed indicated that these filters contributed not more than one-third to the total effect. Confirmatory experiments were done in a chamber into which staphylococci were sprayed: here the walls were treated with a bactericidal solution or the contained air was passed through a bactericidal filter or both. Some graphs of air counts are reproduced showing the effect not only of this treatment but of happenings in the ward such as changing of blankets, arrival of staff, admission of infected patients etc. [No particulars are given of how these solutions are applied, in what quantities, to what, and how often, but in the discussion it is mentioned that whereas air treatment must clearly be continuous, "the basic conditioning process will probably not have to be repeated more than four times annually". The only ingredients in the solutions which seem likely to exert so persistent an effect are salts of silver, zinc and tin.] *L. P. Garrod*

MEDICAL RESEARCH COUNCIL. **Sterilisation by Steam under Increased Pressure. A Report to the Medical Research Council by the Working Party on Pressure-Steam Sterilisers** [HOWIE, J. W., Chairman]. *Lancet.* 1959, Feb. 28, 425–35, 2 figs. [22 refs.]

The Working Party, established in May 1957, whose report this is, made "extensive and detailed investigations into existing arrangements for the sterilisation of surgical equipment in hospital wards, surgical units, sterile-supply departments" and elsewhere, and describe the situation they have found as "unsatisfactory and unsafe".

The report first defines the principles of sterilization by steam under pressure, with particular emphasis on the necessity for removal of air from the chamber, which can be achieved by either downward displacement or a high preliminary vacuum. The commonest faults found are described. As regards equipment these include installation in insanitary or cramped surroundings, poor quality of steam supply, insanitary connexions with service pipes, blocked discharge channels, leakages, and gauges or thermometers out of order. Faults in operation include failure to evacuate air which is only possible by downward displacement when an efficient steam trap is fitted in the discharge channel, overtight packing of drums, incorrect positioning of drums and their contents, incorrect timing (usually undue prolongation of some stage in the run), attempts to sterilize gloves at unduly low temperatures, and re-contamination of the load either by drying with imperfectly filtered air or by insanitary subsequent handling. There are also sections on the sterilization of instruments and of bottled fluids, the testing of sterilizers, and the advantage of fabric "packs" over drums.

Reforms advised include the regular inspection of equipment by engineers, and its operation by staff who understand the process. Drastic recommendations are made about equipment. Sterilizers in which instruments and utensils are boiled should be replaced by high pressure autoclaves in which sterilization can be carried out in a few minutes. Sterilization of water and saline in bulk is unsatisfactory: all such fluids should be autoclaved in bottles. The aim should be to replace older types of autoclave used for packaged equipment (*i.e.* gowns, towels, dressings) with high pre-vacuum high pressure autoclaves automatically controlled: uses may be found for the older instruments in "ward preparation rooms, hospital laboratories, and pharmacies" and elsewhere. *L. P. Garrod*

PENIKETT, E. J. K., ROWE, T. W. & ROBSON, Evelyn. **Vacuum Drying of Steam Sterilized Dressings.** *J. Applied Bact.* 1958, Dec., v. 21, No. 2, 282–90, 5 figs.

The degree of vacuum and time of application needed to dry steam sterilized dressings was investigated. A standard load was used, consisting of towels in a drum. This load was sterilized in an experimental sterilizer, in which precautions were taken to ensure that the steam supplied was dry, for 10 minutes at 20 lb. per sq. in. after an initial vacuum down to 20 mm. Hg. absolute pressure [KNOX and PENIKETT, this *Bulletin*, 1958, v. 33, 605]. At the end of the sterilizing period varying degrees of vacuum were applied, but not maintained. After atmospheric pressure was restored the moisture content of the towels was measured by weighing and by vapour pressure estimation. It was found that a moisture content of 5%, which corresponded to a subjectively dry towel, was obtained after a drying vacuum to 300 mm. Hg. absolute pressure (18 in. Hg. vacuum) for a single drum. For a full load of drums 200 mm. Hg. absolute pressure (21 in. Hg. vacuum) was needed. In these experiments the towels were removed from the drums immediately at the end of the cycle. The authors point out that if drums are used the steam remaining in them will condense on cooling and wet the outside of the dressings. They, therefore, recommend that during the drying stage the absolute pressure should be reduced to 50 mm. Hg. (28 in. Hg. of vacuum) which they found always produces dry dressings.

A second set of experiments was intended to check a hypothesis of HENRY (*J. Applied Bact.*, 1959, v. 22 in press) that steam sterilizing of dressings is an essentially reversible process, given dry saturated steam, complete air removal before sterilizing and complete replacement of steam by air afterwards. He predicted that dressings would have the same moisture content and temperature at the end as at the beginning. Dressings at various initial moisture contents were sterilized at 20 lb. per sq. in. with initial and drying vacua down to 20 mm. Hg. absolute pressure. The final moisture content was then measured. With initial values between 0 and 19% the greatest change observed was 1·5%, and changes of a fraction of 1% were common. This agreed well with Henry's prediction of no change under ideal circumstances.

[The authors emphasize that their drying vacuum was merely attained and was not held. This work confirms the view that prolonged drying times are unnecessary, wasteful and dangerous, and that a failure to dry dressings rapidly indicates a faulty sterilizer or a faulty steam supply.] *J. C. Kelsey*

PUBLIC HEALTH LAB. SERVICE. **The Practical Aspects of Formaldehyde Fumigation.** *Monthly Bull. Ministry of Health & Public Health Lab. Service (directed by Med. Res. Council).* 1958, Dec., v. 17, 270–73.

This is a concise statement of the theory of formaldehyde disinfection, together with practical instructions for it, based on experience at the Microbiological Research Establishment, Porton, and on the work of the Committee on Formaldehyde Disinfection of the Public Health Laboratory Service [this *Bulletin*, 1959, v. 34, 477]. Formaldehyde can be liberated by spraying formalin (when the addition of alcohol is necessary to prevent polymerization), by boiling formalin, or by causing it to boil by adding potassium permanganate. The heating of paraformaldehyde is not recommended because the gas so produced is too dry. A high humidity promotes bactericidal action, as does increase in temperature. Instructions as regards quantities to be used are given for disinfecting rooms, from which fabrics should be removed, for disinfecting small objects (respirators, leather goods, boots and toys) in a chamber, and for disinfecting fabrics, either at normal temperature, when items must be well separated and extra formalin used to compensate for absorption, or in a heated chamber, where some penetration of a packed load will occur. [It is not mentioned here that in the experiments conducted by the Public Health Lab. Service Committee on disinfection in a heated chamber a preliminary vacuum was drawn: this may have been a factor in promoting penetration.] *L. P. Garrod*

## INDIVIDUAL BACTERIA

*In this section the abstracts are arranged as far as possible in the following order: General; Enteric Organisms; Corynebacterium, Mycobacterium; Staphylococcus, Streptococcus; Brucella; Haemophilus; Pasteurella; Pseudomonas; Neisseria; Donovania; Spirochaetes, Leptospira; Anaerobes; Bacillus; Others.*

SILLIKER, J. H. & TAYLOR, W. I. **Isolation of Salmonellae from Food Samples. II. The Effect of Added Food Samples upon the Performance of Enrichment Broths.** *Applied Microbiol.* Baltimore. 1958, July, v. 6, No. 4, 228–32.

The selectivity for salmonellae of selenite and tetrathionate enrichment broths is impaired by the presence of small amounts of certain foodstuffs and when large samples such as egg products and gelatin require examination dilution alone is inadequate to remove this effect.

It was found that greatly improved cultural results could be obtained by 10-fold dilution of the foodstuff in buffered water and centrifugation at 1,100 *g* for 10 minutes in an angle centrifuge followed by growth in enrichment broth.

The degree of impairment of selectivity was found to be directly proportional to the amount of soluble material in the sample and it is suggested that the same action may also affect the isolation of salmonellae from pathological material. *J. Nagington*

WESTPHAL, O., LÜDERITZ, O., STAUB, Anne M. & TINELLI, Regina. Vorkommen und immunologische Differenzierung zweier optischer Antipoden - Abequose und Colitose (3-Desoxy-D- und -L-fucose)- als determinate Endgruppen in *Salmonella*-O-Antigen. [**Demonstration and Immunological Differentiation of Two Optical Antipodes - Abequose and Colitose (3-Deoxy-D- and -L-fucose)- as Determinant Endgroups in** *Salmonella* **O Antigens**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 5/6, 307–14. [29 refs.]

FUKASAWA, T. & NIKAIDO, H. **Formation of " Protoplasts " in Mutant Strains of** *Salmonella* **induced by Galactose.** [Correspondence.] *Nature.* 1959, Apr. 18, v. 183, 1131–2, 2 figs.

COSTA, G. A. & VILLELA, G. G. **Oxidation of L-glutamic Acid in Relation to Antigenic Composition of** *Salmonella typhi. Proc. Soc. Exper. Biol. & Med.* 1959, Apr., v. 100, No. 4, 714–6, 4 figs.

NICOLLE, P., DIVERNEAU, Gisele & BRAULT, Jacqueline. Relation entre les divers états lysogènes du type A de *Salmonella typhi* et ses sous-types tels qu'ils sont mis en évidence par une lysotypie complémentaire. [**A Complementary Phage-typing Scheme for** *Salmonella typhi* **Type A and the Lysogenicity of the Sub-types**] *Bull. Res. Counc. of Israel.* 1958, June, v. 7E, Nos. 1/2, 89–100. [33 refs.]

The value of phage-typing *Salmonella typhi* is much reduced by the great frequency of type A, which in parts of the world such as Israel and parts of Africa is almost the only type encountered.

In order further to subdivide type A strains the authors have collected a set of 8 phages, 6 of which are non-Vi phages (1, 2, 3, 4, 6, 7), 1 is a Vi-phage (5) and 1 is Craigie's phage Vi III (8).

These phages enable type A to be divided into 9 subtypes: Coquilhatville, Montreal, Tananarive, Douala, Chamblee, Welshpool, Oswestry, Leopoldville and Maracaïbo.

2 of the sub-types are constantly lysogenic and the remainder are less constantly so except for Tananarive and Oswestry, of which lysogenic strains have not yet been demonstrated. The sensitivity of the 9 sub-types to these phages produces a corroborative method of classification as each phage has a characteristic host range and only the phages from Montreal and Leopoldville give the same pattern. *J. Nagington*

FEELEY, J. C., SWORD, C. P., MANCLARK, C. R. & PICKETT, M. J. **The Use of Formalin-Preserved Erythrocytes in the Enterobacterial Hemagglutination Test.** *Amer. J. Clin. Path.* 1958, July, v. 30, No. 1, 77–82.

Details are given of a method of preservation of human erythrocytes by formalin which is based on the technique described by Cox, this *Bulletin*, 1957, v. 32, 10.

Salmonella and other enterobacteriaceae antigens were prepared by heating cultures for 1 hour at 100°C. The formalized erythrocytes were sensitized by incubation with one or more of these antigens for 1 hour at 37°C., washed and then used as a 1% suspension for haemagglutination tests in which the readings were taken from the pattern of deposited cells.

The formalized cells were stable in stock suspensions for over 1 year. They retained their ability to adsorb bacterial antigens and showed no tendency to spontaneous agglutination during this period. Sensitized erythrocytes were suitable for use for at least 300 days. Such sensitized cells are appreciably more stable than fresh erythrocytes sensitized without formalin treatment. *J. Nagington*

LAMBIN, S., GERMAN, A. & SIGRIST, W. Influence de la lyophilisation sur les constituants et le pouvoir antigéniques d'*E. typhosa* et de *S. paratyphi* B. [**Influence of Lyophilization on the Constituents and Antigenic Power of** *Salmonella typhi* **and** *Salm. paratyphi B*] *C.R. Soc. Biol.* 1958, v. 152, No. 12, 1650–53.

The antigenic constitution of the typhoid-paratyphoid organisms was examined after a single freeze-drying process and also after successive freeze-drying processes. The cultures employed were: a strain of *Salmonella typhi* rich in Vi-antigen and another poor in Vi-antigen, a strain of *Salm. paratyphi* A and a strain of *Salm. paratyphi* B. They were suspended in Stamp's gelatin medium and lyophilized in an Edwards' drying machine and subsequently tested for agglutinability, agglutinogenicity and protective effect as vaccines.

It was found that a single drying had no obvious effect on the O or Vi antigens of *Salm. typhi*, and little on the H antigen, although the last named was apt to give atypical agglutination. When, however, the organisms were subjected to repeated drying (many times) over a comparatively short period the activity of the H and Vi antigens gradually fell off but the O antigen was completely unaffected. This stability of the O antigen was also noted in heat-killed suspensions, even after they had been freeze-dried some 15 times. Similar results were obtained with the paratyphoid strains. *H. J. Bensted*

BENSTED, H. J. **Colony Variation and Mouse Virulence of Typhoid Bacilli.** *Bull. Res. Counc. of Israel.* 1958, June, v. 7E, Nos. 1/2, 25–30.

Experiments are described which took place in 1932. At that time the Rawlings strain of *Salmonella typhi* was widely used in TAB vaccines and it had become so rough that it was felt that it should be replaced.

That year there was an outbreak of typhoid at Malton, Yorkshire and a number of freshly isolated strains of the causative organism were injected intraperitoneally into mice to assay their virulence. It was found that although apparently completely smooth colonies were selected the strains differed from one another by as much as 5 times in their minimal lethal doses, and in one instance this difference was found with strains from the same patient. But the organisms recovered from the spleens of the mice were of a uniformly high virulence with an MLD of $50 \times 10^6$ bacteria.

The rough Rawlings strain was then passaged in the same way and from mice given the MLD of $500 \times 10^6$ bacteria smooth colonies were grown from the spleens which were not agglutinated by O serum, had an MLD of $50 \times 10^6$ and had more than 6 times the protective value as a vaccine.

This work led to the description of the Vi antigen by Felix and its quantitative relationship with O-inagglutinability and mouse virulence. *J. Nagington*

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Hirsch, W. & Hornstein, Lea. **The Effect of Chloroform Vapours on the Vi Antigen and on the O Resistance of *Salmonella typhi*, and the Application of this Effect to Plate Agar Cultures.** *Bull. Res. Counc. of Israel.* 1958, June, v. 7E, Nos. 1/2, 61–6. [12 refs.]

Chloroform vapour destroys the O-inagglutinability of colonies of Vi strains of *Salmonella typhi* and also causes loss of Vi-agglutinability.

To demonstrate this, 2 disks of filter paper are fitted into the lid of the petri dish and soaked with chloroform. The lid is replaced over the culture, the plate inverted and incubated at 37°C. in a tightly closed jar.

The removal of O-inagglutinability usually takes about 15–30 minutes, but it may require up to 1 hour with such rich Vi strains as Ty2.

The disappearance of Vi agglutinability is slower and usually requires 1–3 hours and in highly Vi strains 6–24 hours. Agglutination by 0·2% trypaflavine is abolished more rapidly than this.

The same results can be achieved by other organic solvents and it may be associated with the lipoid fraction of the Vi antigen. *J. Nagington*

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Jude, A. Role des antigènes O et Vi dans l'immunisation de la souris contre le bacille typhique. [**The Action of O and Vi Antigens in the Immunization of Mice against** *Salmonella typhi*] *Bull. Res. Counc. of Israel.* 1958, June, v. 7E, Nos. 1/2, 69–76, 2 figs. [30 refs.]

In a series of active-protection tests mice were vaccinated with a single subcutaneous constant dose of heat-killed vaccine and challenged 10 days later by intraperitoneal injection with varying doses of *Salmonella typhi* Ty2.

Those vaccinated with O antigen, either of *Salm. typhi* or *Salm. pullorum* had a resistance little different from unvaccinated controls.

Vaccination with Vi antigen gave a significant increase in resistance even when the Vi antigen was that of a Ballerup strain.

But maximum resistance was achieved only by vaccination with both O and Vi antigens. This could be either by injection of the homologous antigens as in Ty2 vaccine or by one homologous and one heterologous, *e.g. Salm. typhi* 0901 (O) and Ballerup (Vi) or by both heterologous antigens, *e.g. Salm. pullorum* (O) and Ballerup. *J. Nagington*

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Landy, M. **Observations on the Immune Response of the Mouse to Vi Antigen.** *Bull. Res. Counc. of Israel.* 1958, June, v. 7E, Nos. 1/2, 77–88, 1 fig. [19 refs.]

Purified Vi antigens derived from *Escherichia coli* and a Ballerup strain actively immunize mice but O antigen from *Salmonella typhi* 0901 gives little or no protection against challenge with the Vi strain of *Salm. typhi* Ty2.

Immunity after intraperitoneal injection of 1·0 μgm. of Vi antigen develops rapidly. It is first detectable, by active protection tests, in 36 hours. At 48 hours about one-half the final protection is reached and the maximum level is reached in 66–72 hours. Serum Vi antibody is only detectable at 72 hours and thereafter.

Heat-killed, phenol-preserved O vaccine made from *Salm. typhi* 58 also gives early protection and as this protective property can be removed from serum by adsorption with Vi-coated erythrocytes it is assumed also to be due to Vi antibody.

This rate of development of specific immunity is more rapid than has been observed in mice after injection of antigens other than Vi. It is independent of the route of injection, is parallel with the production of protective antibody and persists for many weeks.

It is considered to be unique and distinct from the rapidly developed, transitory non-specific increase in resistance produced by various Gram-negative organisms, including *Salm. typhi* or their somatic antigens.

*J. Nagington*

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Rappaport, F. & Konforti, N. **Selective Enrichment Medium for Paratyphoid Bacteria. Inhibitory and Growth Promoting Factors.** *Applied Microbiol.* Baltimore. 1959, Mar., v. 7, No. 2, 63–6. [26 refs.]

In drawing attention to the superiority of Bacto-Tryptone malachite green magnesium chloride medium [this *Bulletin*, 1957, v. 32, 74] as an enrichment medium for the isolation of *Salmonella paratyphi* B the authors discuss the roles played by the dye and the magnesium salt. In the first place they find that salmonellae grow equally well in Bacto-peptone and Bacto-Tryptone simple media, but when malachite green and magnesium chloride are added for enrichment purposes the good effect is obtained only if Bacto-Tryptone is used. Malachite green has a toxic effect on bacteria; this is counteracted by the presence of magnesium chloride and it is suggested that these 2 ingredients synergistically inhibit ordinary faecal contaminants (*Escherichia coli, Pseudomonas pyocyanea*, etc.) while not affecting the salmonellae the growth of which is enhanced by the Bacto-tryptone.

[While this may be true for *Salm. paratyphi* B all salmonella organisms may not be equally affected.]

*H. J. Bensted*

MANDEL, A. D., BARON, L. S. & BUCKLER, C. E. **Role of Vi Antigen in** *Salmonella paratyphi* **C Infections.** *Proc. Soc. Exper. Biol. & Med.* 1959, Mar., v. 100, No. 3, 653–6.

Mouse-virulence of *Salmonella typhi* and the mouse-protective properties of typhoid vaccines are directly related to the amount of Vi-antigen in the culture of *Salm. typhi* tested or in the particular vaccine used. This was established by FELIX and PITT in 1934 [this *Bulletin*, 1934, v. 9, 562] and it was subsequently shown that Vi-antibody derived from other organisms would protect mice against a challenge with virulent typhoid bacilli. This paper describes experiments on the same lines with *Salm. paratyphi* C. Although the authors were able to show that Vi-positive cultures of paratyphoid C were more virulent for mice than Vi-negative cultures they were unable to demonstrate any protective effect of the Vi-antigen against infections in mice with *Salm. paratyphi* C. Active protection tests with heat-killed vaccines of Vi-positive and Vi-negative cultures showed no difference; animals immunized with acetone-killed suspensions of Vi-positive cultures (this treatment preserved the Vi-antigen) were not protected against a paratyphoid C challenge and the purified Vi-antigen prepared from *Escherichia coli* 5396/38 was equally without effect. The authors failed to observe the temporary protection afforded against the high dose challenge described by ARCHER and WHITBY [*ibid.*, 1958, v. 33, 382]. An anti-paratyphoid C rabbit serum, prepared from a Vi-positive culture of *Salm. paratyphi* C, did not protect mice against a homologous challenge, but it afforded adequate protection to a parallel group of mice challenged with *Salm. typhi* Ty2.

[It would appear from the results presented in this paper that the role of Vi-antigen in *Salm. paratyphi* C infections in mice remains obscure. Although the authors used young mice, 10–12 grammes, in their virulence tests and recorded a lower LD50 for Vi-positive than for Vi-negative cultures the results were irregular. It is clear that even if the Vi-antigen has any protective effect against paratyphoid C infections in mice, as distinct from the protective effect against the toxic manifestations of high challenge doses (ARCHER and WHITBY), other assessment methods will have to be developed before this can be demonstrated. There appears to be no significant multiplication of *Salm. typhi* in the mouse, at any rate when mucin is not used, whereas extremely small doses of *Salm. paratyphi* C can invade and multiply in a manner not dissimilar to *Salm. typhi-murium*, which does not carry any Vi-antigen.]

*H. J. Bensted*

GERICHTER, C. B., EVENCHIK, Z. & SILBERSTEIN, W. **The Effect of Storage Temperature on the Potency of T.A.B. Vaccine.** *Bull. Res. Counc. of Israel.* 1958, June, v. 7E, Nos. 1/2, 53–60.

The effect of temperature on alcohol-killed, alcohol-preserved TAB vaccine was measured by titration of its potency at intervals by means of active-protection tests in mice.

Vaccine showed a loss of potency after more than 1 week at 20°C., more than 2 days at 28°C. and 16 hours at 37°C. Vaccine stored at 2–4°C. retained its potency.

After the initial drop the potency of the vaccine reached a level which declined only slightly with continued storage. This level was reached after 2 weeks at 20°C., slightly earlier at room temperature (18–28°C.), after 4 days at 28°C. and 2 days at 37°C.

*J. Nagington*

HUGHES, M. H. *Salmonella* **Infections in Accra, Ghana, West Africa.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1958, July, v. 52, No. 4, 377–82. [13 refs.]

During a period of 2½ years in 1952–5, 451 salmonella strains were isolated at Accra, Ghana. There were 47 serotypes of which 3 were new ones. The majority of these strains came from patients with enteric-type fevers and multiple infections were common [see also HUGHES, this *Bulletin*, 1956, v. 31, 501].

The most common serotypes were *Salmonella typhi* (245 strains), *Salm. paratyphi A* (45), *Salm. paratyphi C* (27), Salm. Virchow (21), *Salm. typhi-murium* (17) and Salm. Dublin (7). Only 10 strains came from animal sources—Salm. Dublin (4) from cattle, *Salm. typhi-murium* (2), *Salm. paratyphi C* (1), Salm. Virchow (1), *Salm. anatum* (1) from poultry and 1 strain of Salm. Rubislaw from a dog.

This survey suggests that salmonella infections are very frequent among all classes in West Africa. It is thought that most of the infections are food-borne, probably mainly through faecal contamination, and it is likely that infected poultry may also play an important part.

*J. Nagington*

BROWNING, P. M. H., MOORE, J. M. & STEVENSON, J. S. **A New** *Salmonella* **Type: Salmonella Glasgow.** *J. Path. & Bact.* 1959, Apr., v. 77, No. 2, 650–51.

"A description is given of a new Salmonella type isolated from an infant and an adult; the organism produced only mild illness. The antigenic structure of the new type is represented by the symbols 16 : *b*—1, 6; the proposed name of the organism is *Salmonella glasgow*."

HOFMANN, S. & HERRLER, H. Ein neuer *Salmonella*-Typ: S. Friedrichsfelde (28 : f,g : –). **[A New** *Salmonella* **Type, Salm. Friedrichsfelde, 28 : f,g:–]** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 5/6, 303–4.

ROHDE, R. & BISCHOFF, J. Ein neuer *Salmonella*-Typ (S. Harburg) aus ausländischem Fischmehl. **[A New *Salmonella* Type, Salm. Harburg, from Imported Fish Meal]** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 5/6, 305–6.

KIRSCHE, P., LE MINOR, L., LE MINOR, S., KHOURY, B. & DRÉAN, D. Un nouveau sérotype de *Salmonella*, S. Niamey. **[A New *Salmonella* Serotype: Salm. Niamey]** *Ann. Inst. Pasteur.* 1959, May, v. 96, No. 5, 642.

EDWARDS, P. R., LE MINOR, L. & FIFE, Mary A. **Six New Arizona Types recovered from Normal Reptiles (1,4 : 24–38; 1,4 : 29–28; 1,33 : 23–21; 1,33 : 24–25; 5 : 24–28; and 5 : 26–31).** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 5/6, 348–51.

CARPENTER, K. Patricia & LACHOWICZ, K. **The Catalase Activity of *Shigella flexneri*.** *J. Path. & Bact.* 1959, Apr., v. 77, No. 2, 645–8. [18 refs.]

"Of 500 *Shigella flexneri* strains tested qualitatively for their catalase activity, 24 were catalase-negative. Of these, 19 belonged to serotype 4*a*, 1 to serotype 6, and 4 to the Y variant, but these last four strains were selected laboratory variants of known 4*a* serotype strains. It is suggested that the catalase reaction of *Sh. flexneri* strains may be of value epidemiologically."

ROBBINS, Mary L., PARR, L. W. & HANN, W. D. **Coliform-*Shigella* Antagonism in Fecal Cultures among Isolates from Residents of two Egyptian Villages.** *Amer. J. Hyg.* 1958, July, v. 68, No. 1, 6–12. [13 refs.]

13 shigella strains (8 *Shigella dysenteriae*, 4 *Sh. flexneri* and 1 *Sh. sonnei*) were grown from rectal swabs of Egyptian villagers with diarrhoea. They were examined for inhibition by coliform organisms by inclusion in pour-plates and the coliform organisms spotted on to the surface. It was found that coliforms inhibitory to them were obtained most frequently from the patients' own flora (4 of the 13), followed by family contacts and less often from close neighbours. Only a few inhibitory strains were grown from distant non-contacts.

No relationship was found between diarrhoea and the presence of coliform organisms inhibitory to a highly susceptible indicator strain of *Sh. flexneri* type 3.

Although the series is so small it is suggested that exposure to a shigella strain may cause an increase in gut organisms which are inhibitory to it.

*J. Nagington*

RAUSS, K. & VERTÉNYI, A. Ein coliformes Bakterium mit *Sh. flexneri*-verwandten Antigeneigenschaften. **[A Coliform Bacterium containing an Antigen related to *Sh. flexneri*]** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 5/6, 352–6. [10 refs.]

PIERFITTE, M. Comparaison d'une souche de *Escherichia coli* sulfamido-sensible et d'une souche sulfamido-résistante : composition des protéines en acides aminés. **[Comparison of Strains of *Escherichia coli* Sensitive and Resistant to Sulphonamides in Relation to the Amino Acid Composition of the Proteins]** *C.R. Soc. Biol.* 1959, v. 153, No. 1, 147–50. [11 refs.]

There was no appreciable difference in the amino acids.

CRAWFORD, L. V. **Nucleic Acid Metabolism in *Escherichia coli* infected with Phage T5.** *Virology.* New York. 1959, Apr., v. 7, No. 4, 359–74, 7 figs. [21 refs.]

SEKIGUCHI, M. & TAKAGI, Y. **Synthesis of Deoxyribonucleic Acid by Phage-Infected *Escherichia coli* in the presence of Mitomycin C.** [Correspondence.] *Nature.* 1959, Apr. 18, v. 183, 1134–5, 1 fig.

LINO, A. Prime ricerche intorno alla purificazione di una delle fosfatasi acide dell'*E. coli.* **[Preliminary Studies on the Purification of an Acid Phosphatase of *Escherichia coli*]** *Atti Soc. Peloritana Sci. Fis. Mat. Nat.* Messina. 1957–58, v. 4, Nos. 3/4, 263–7.

LINO, A. Circa la presenza di un'attività fosfotransferasica nell'*Aerobacter aerogenes.* **[The Presence of Transphosphorylase Activity in *Aerobacter Aerogenes*]** *Atti Soc. Peloritana Sci. Fis. Mat. Nat.* Messina. 1957–58, v. 4, Nos. 3/4, 303–6, 2 graphs.

WEISSBACH, A.; HURWITZ, J. **The formation of 2-Keto-3-Deoxyheptonic Acid in Extracts of *Escherichia coli* B. I. Identification** [WEISSBACH & HURWITZ]. *J. Biol. Chem.* 1959, Apr., v. 234, No. 4, 705–9, 2 figs. [23 refs.] **II. Enzymic Studies** [HURWITZ & WEISSBACH]. *Ibid.*, 710–12.

STILLWELL, E. F., MARONEY, S. P., Jr. & WILBUR, K. M. **Effect of Irradiated Fatty Acids on the Growth of *Escherichia coli*.** *J. Bacteriology.* 1959, Apr., v. 77, No. 4, 510–11, 3 figs.

KELNER, A. & JACOBS, L. L. **Ultraviolet-Induced Abnormal Growth in *Escherichia coli*; the Influence of Yeast Extract and of Photoreactivation.** *J. Bacteriology.* 1959, Mar., v. 77, No. 3, 281–95, 9 figs. [34 refs.]

IYER, V. N. & SZYBALSKI, W. **Mutagenic Effect of Azaserine in relation to Azaserine resistance in *Escherichia coli*.** *Science.* 1959, Mar. 27, v. 129, 839–40, 1 fig.

McKay, E. & Smith, J. **A Small Outbreak of Neonatal Meningitis in a Maternity Unit.** *Arch. Dis. in Childhood.* 1958, Aug., v. 33, No. 170, 358–61.

An outbreak of meningitis is described in which 3 infants, 2 of which were twins, were affected. All had been delivered at the same maternity hospital within a period of 2 months. They became ill 6, 11 and 14 days after birth. One died and both survivors had residual neurological damage.

From the cerebrospinal fluids of each infant was cultured an organism which resembled *Escherichia coli* more closely than any other member of the enterobacteriaceae. Biochemically it differed from it in that it did not ferment lactose, fermented adonitol and inositol, grew in Koser's citrate, produced $H_2S$ and utilized urea (late). The strains were not related to *E. coli* serotypes 1–137 and were considered to be " intermediate coliforms ".

The same organism was cultured from the faeces of the 3 infants but no indication of its original source was found and it was not found subsequently in 1,500 routine specimens of faeces examined. *J. Nagington*

Brody, J. A., Moore, Helen & King, Elizabeth O. **Meningitis caused by an Unclassified Gram-Negative Bacterium in Newborn Infants.** *J. Dis. Children.* Chicago. 1958, July, v. 96, No. 1, 1–5.

In a period of over a year in 1956–7 in 2 maternity units in the U.S.A. 19 newborn infants, 17 of which were premature, developed meningitis. 15 died, 3 survivors had hydrocephalus and only 1 made a complete recovery.

A Gram-negative bacillus was cultured from the blood or cerebrospinal fluid or both in nearly all cases and 7 strains were studied in detail. The organism ferments carbohydrates only after 7 days incubation in a nutrient broth base. It ferments lactose, glucose, maltose and mannitol but not sucrose or xylose. It is oxidase-positive, and a weak indole producer. It is urease, nitrate, MR and VP-negative. Only high concentrations of erythromycin and carbomycin were inhibitory *in vitro*. It is a long filamentous non-motile rod. Attempts to classify it have so far been unsuccessful.

The organism was recovered on 5 occasions from the throats of 4 healthy babies immediately after the outbreak period and they continued symptom-free. After this it could not be found again in the hospital environment. *J. Nagington*

Soman, D. W. & Patel, K. K. C. **Comparison of Toxigenicity Tests of *C. diphtheriae* by Three Different Methods.** *Indian J. Med. Sci.* 1958, Apr., v. 12, No. 4, 235–41. [24 refs.]

89 *Corynebacterium diphtheriae* strains were tested by guineapig inoculation, by injection to chick embryo and by the Elek agar diffusion *in vitro* test. Results were identical by all 3 methods, 81 strains being found virulent.

In view of all this the plate diffusion method which is the simplest and cheapest should be used normally. Investigation of modification of the constitution of the medium recommended for this test showed that proteose peptone although as claimed, the best, could be satisfactorily replaced by bacto peptone in the presence of meat extract.

A test of 6 different varieties of serum as medium constituents showed human to be the best and sheep, rabbit, ox and horse to be less good. *J. W. McLeod*

Kuhns, W. J., Masouredis, S. P. & Swabey, L. **Characterization of Complexes which contain Diphtheria Toxin and Human Nonprecipitating Antitoxin.** *J. Immunology.* 1959, Mar., v. 82, No. 3, 226–31, 2 figs. [20 refs.]

" Complexes which contained nonprecipitating diphtheria antitoxin and $I^{131}$ toxin were analyzed for sedimentation behaviour in the ultracentrifuge. When high-speed centrifugation was employed using a separation cell, it was found that sedimentation of the complex was fastest at six-fold antibody excess and slowest at antibody equivalence as judged by relative percentages of $I^{131}$ in upper and lower portions of the cell. When studied electrophoretically using the technique of zone electrophoresis, it was found that complexes at equivalence or in antibody excess remained close to the point of application, but migrated toward the anode when in antigen excess. Approximate sedimentation constants for the different toxin-antitoxin combinations are presented. The use of labelled antigens and physicochemical methods in the purification of nonprecipitating antibody are discussed."

Tinne, J. E. **A Methylene Blue Medium for distinguishing Virulent Mycobacteria.** *Scottish Med. J.* Glasgow. 1959, Mar., v. 4, No. 3, 130–32. [16 refs.]

Bloch (*Amer. Rev. Tuberculosis*, 1950, v. 61, 270) showed that whereas virulent tubercle bacilli took more than 1 hour to decolorize methylene blue, avirulent strains, *e.g.* BCG, decolorized it in less than 15 minutes, and the saprophytes took only 3 minutes or less.

In the present paper the author reports that 0·02% methylene blue added to Löwenstein-Jensen medium enables tubercle bacilli to be readily differentiated from the saprophytes. On this medium Gram-negative bacteria bleach the medium, but Gram-positive bacteria are non-reducers, except the less pathogenic mycobacteria. The tubercle bacilli grow as dark indigo colonies on the sky blue medium. For reduction to occur the caps of the bottles have, however, to be tightly closed and the colour returns when the caps are loosened.

[The author states that the use of this medium enables dehydrogenase activity to be easily detected and that its detection forms a simple alternative to the use of guineapigs for demonstrating virulence. The table of results, however, shows that 3 isoniazid-resistant strains of tubercle bacilli which produced in guineapigs only local lesions at the injection site, were indistinguishable from 25 virulent strains; the only mycobacteria in the table to bleach the medium were the saprophytes.] *S. R. M. Bushby*

WECHSELBERG, K. *In vitro*-Studien über den Einfluss öliger Pflanzenextrakte aus *Tropaeolum maius, Cochlearia armoracia* und *Allium sativum* auf das Wachstum von Tuberkelbakterien. [*In vitro* **Studies on the Effect of Oils Extracted from** *Tropaeolum maius, Cochlearia armoracia* **and** *Allium sativa* **on the Growth of Tubercle Bacteria**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 4, 380–94. [Numerous refs.]

The first 3 references in this paper are to publications in the years 1561, 1719 and 1780, although a good deal more recent work is quoted later on the antibacterial activity of old herbal remedies, or what are now sometimes referred to as "antibiotics from higher plants". The author has tested the effect of the essential oils of nasturtium, horse radish and garlic on the growth of tubercle bacilli by 2 methods. The "gas test" consists of exposing cultures on a solid medium in a sealed chamber of 50 ml. capacity in which different volumes of the essential oil are placed and allowed to volatilize. Nasturtium oil had a very powerful inhibitory effect: horse radish caused delayed and diminished growth, and garlic had no effect at all. In the other method the oils were added in different amounts together with an emulsifying agent to a liquid medium: no inhibition was produced at any concentration by any of them, and this is attributed to inactivation by proteins in the medium. By the gas test a synthetic "benzyl mustard oil" was much more active than nasturtium oil, in which this substance is said to be the active constituent. *L. P. Garrod*

NUTTER, J. E., GEMMILL, C. L. & MYRVIK, Q. N. **The Influence of 3,3$^1$,5-Triiodo-L-Thyronine on the Survival Time of Mice with Tuberculosis and Pneumococcosis.** *Amer. Rev. Tuberculosis.* 1959, Mar., v. 79, No. 3, 339–43, 2 figs. [11 refs.]

The triiodothyronine was administered to the mice in their drinking water and the effects on the metabolic rates, which were determined by the closed method of GEMMILL, ranged from an undetectable increase with the concentration of 3 μgm. triiodothyronine per ml. of drinking water to a 140% increase with 24 μgm. per 100 ml.

In the groups of mice infected intravenously with the Ravenel strain of tubercle bacilli, concentrations of 3 and 6 μgm. triiodothyronine per 100 ml. for 16 days before and throughout the infection did not decrease the survival time but concentrations of 12 and 24 μgm. per 100 ml. significantly reduced the 50% survival time from 33 days to 22·5 and 21 days, respectively; decreasing the period of pretreatment to 2 days did not alter the effects of the treatment. Gross examination did not reveal any difference in the lungs of the treated and untreated animals.

In the acute experiments with the pneumococcus, in which the 50% survival time of the untreated animals was 28 hours, 3 μgm. triiodothyronine per 100 ml. had no effect on the survival time but 6, 12 and 24 μgm. per 100 ml. decreased this survival time to 24, 22·5 and 20·5 hours, respectively, when treatment was given for 8 days before infection, but only 24 μgm. per 100 ml. had a similar significant effect when treatment was for only 4 days before infection; the 50% survival time was then reduced from 23·5 days to 16·5 days. Untreated mice show a neutrophil leucocytosis during the infection but those on treatment showed only a small increase in mature cells and no increase in young cells.

These results are in agreement with those of some other workers [this *Bulletin*, 1955, v. 30, 543; 1956, v. 31, 673] but in conflict with those of others [*ibid.*, 1956, v. 31, 945]. In the opinion of the authors, triiodothyronine is involved in multiple pathways associated with the physiology of resistance, and its effect in the resistance of man to infections remains unanswered. *S. R. M. Bushby*

KITAZAWA, Y. & OHTA, S. **Investigation of the Influence of Antimicrobial Drugs on the Allergic Reaction to Reinfection Tuberculosis in Rabbits.** *Amer. Rev. Tuberculosis.* 1959, Mar., v. 79, No. 3, 329–38, 6 figs.

"When rabbits are reinfected by *Mycobacterium tuberculosis*, whose growth ability has been weakened by PAS or isoniazid, and by resistant bacilli, whose growth ability has been weakened just by keeping them in water, a decrease in the tuberculin reaction appears. By contrast, in the case of a tuberculous infection treated by water or streptomycin, the hypersensitive reaction is preserved to a weaker degree than in an untreated infection.

"Primary infection by any of these bacilli gives a milder infection than primary infection by living bacilli, thus proving that there is a decrease in pathogenicity. However, although the decrease of growth ability and the decrease of antigenicity are parallel, antigenicity is preserved in the case of heat-killed bacilli.

"It is assumed that the above fact can easily explain the nonexistence of generalized tuberculin reactions, such as the Jarisch Herxheimer reaction in syphilis, that might be caused by tuberculin released from destroyed bacilli in a lesion during chemotherapy. Furthermore, it is worth while noting that the typical Koch phenomenon was produced by the resistant bacilli which were used for the above test."

FRAPPIER, A., PORTELANCE, V. & ST.-PIERRE, J. **Some Biologic Properties of Mycobacteria following the Extraction of Lipids. The Power to initiate Acquired Resistance.** *Amer. Rev. Tuberculosis.* 1959, Mar., v. 79, No. 3, 296–306. [14 refs.]

This paper is concerned with the immunizing properties for guineapigs of saline suspensions of bacillary residues of BCG and H37Rv from which the lipids have been progressively more fully extracted. The BCG was extracted by the method of MACHEBOEUF *et al.* (*Ann. Inst. Pasteur.*, 1935, v. 54, 71), and yielded 5 progressively more extracted residues. In this method the bacilli are exposed to organic solvents for prolonged periods, whereas the H37Rv was extracted by 2 rapid extraction methods—1 was by the acetone and ether method of MACHEBOEUF and DIERYCK (*C.R. Acad. Sci.*, 1936, v. 202, 164) and the other by alcohol and ether followed by chloroform.

Groups of guineapigs were injected with various doses of the antigens and tested 3 months later with tuberculin. The animals were then challenged with 0·00001 mgm. of the Ravenel strain, a dose that gave a median survival time of 124-160 days in unimmunized animals. The protective effect of vaccines was assessed by the effect on the survival time and the extent of the tuberculosis as compared with the effects of vaccinating with living BCG. The extent of the disease was expressed numerically, based on the number of lesions on the surface of the lungs, liver and spleen, and the significance of the difference between the groups was measured by the chi-square test.

In the first experiments, 6 scarifications with 13 mgm. of No. I BCG residue per ml. produced a positive tuberculin reaction in only 22% of the animals and had no significant effect on the disease. The experiment also showed that 6 scarifications with 3 mgm. of living BCG per ml. gave some protection which was not proportionally increased by increasing the concentration of the BCG and was not enhanced by adding the No. I residue to the vaccine.

In the second experiment, attempts were made to immunize with more massive doses of the antigens. 20 mgm. of equal parts of residues I and II were injected intraperitoneally into 1 group and 15 mgm. of equal parts of the residues III, IV and V were injected into another group. Each group was then further vaccinated during the next week by a series of 6 scarifications followed 5 days later by a similar series of scarifications. The results showed that these residues afforded insignificant protection as compared with that by living BCG or that by 90 mgm. intraperitoneally plus 180 mgm./ml. by scarification of heat-killed BCG, and only 47% of the 1st group and 29% of the 2nd group became tuberculin-positive. However, in the opinion of the authors, the feeble challenge dose and the relatively small numbers of animals that survived the duration of the experiment probably minimized the differences between the vaccinated and the control groups, and thus indicated the difficulty of detecting immunity by such small challenge doses.

The third experiment was with the residues of H37Rv. The total dose of these residues used was 25 mgm. injected in 5 doses, the first being given intraperitoneally and the others subcutaneously at 4-day intervals. Both of the vaccines afforded some protection but less than that afforded to a third group of animals vaccinated with living BCG; both residues also produced approximately 80% of tuberculin conversions. In this experiment were also included groups of animals vaccinated with a filtrate of an old BCG culture and mechanically disrupted BCG; both of these vaccines enhanced the disease.

Thus, only the residues of the rapidly extracted H37Rv and the heat-killed BCG afforded protection in these experiments, but the protection was less than that afforded by living BCG. *S. R. M. Bushby*

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CARPENTER, C. M., NAYLOR-FOOTE, A. W. C., TAPLIN, G. V., LAWRENCE, C. A. & DRAKE, C. L. **Preliminary Report on Vaccines prepared from Gamma-Irradiated** *Mycobacterium tuberculosis* **and** *Brucella suis*. *Amer. Rev. Tuberculosis.* 1959, Mar., v. 79, No. 3, 374–7, 1 fig.

SARBER *et al.* [this *Bulletin*, 1951, v. 26, 141] have produced effective immunization with irradiated organisms and although high energy irradiation inactivates bacteria, much of the effect of these particles is probably due to secondary effects produced in the suspending medium. The present preliminary communication reports effective inactivation of tubercle bacilli and *Brucella suis* in the lyophilized state by exposing sealed ampoules of the bacteria to gamma radiation from $^{60}$Co. After this exposure the organisms respired but did not multiply or produce disease when injected into animals, and their potential immunizing properties were shown in mice and guineapigs challenged with viable bacilli.

The irradiated brucella vaccine protected 85% of the mice compared with 40% protected by a heat-killed vaccine when subsequently challenged. This vaccine was also shown to stimulate a higher titre of agglutinins in rabbits than the killed vaccine, the titres being 1 : 5,120 and 1 : 1,280 respectively.

In the mouse experiments with the irradiated H37Rv vaccine, the immunity was judged by the average weight of the lungs 57 days after challenge with intravenous living H37Rv, given 35 days after vaccination; $6 \times 10^7$ irradiated bacilli, injected intraperitoneally, gave immunity equal to that given by one-half the number of living BCG. Immunity was also demonstrated in guineapigs vaccinated subcutaneously with 0·2 ml. of a suspension containing $6 \times 10^8$ bacilli per ml. and challenged with 0·1 mgm. H37Rv, but of especial interest was the observation that the tuberculin reaction was often weak or negative in the protected animals.

These vaccines are being further examined and it is hoped that they will not show the antigenic changes known to occur with attenuated or heat-killed organisms. *S. R. M. Bushby*

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PATNODE, R. A. & HUDGINS, P. C. **Sonic Fragility of Leukocytes from Guinea Pigs vaccinated with BCG.** *Amer. Rev. Tuberculosis.* 1959, Mar., v. 79, No. 3, 323–8. [12 refs.]

"Immune monocytes (from guinea pigs vaccinated with heat-killed tubercle bacilli in paraffin oil) suspended in immune serum were significantly more resistant to disruption by sonic vibration than similar cells in normal serum. Suspending normal cells in immune serum did not increase their resistance to sonic disruption.

"Marked resistance to sonic disruption was first detected in monocytes of guinea pigs vaccinated with BCG collected twelve days after vaccination.

"When thoroughly washed immune monocytes were suspended in normal serum and incubated for six hours, a factor was released into the serum capable of protecting normal monocytes against sonic disruption and of rendering normal monocytes susceptible to lysis by PPD.

"When normal monocytes were suspended in serum collected from BCG-vaccinated guinea pigs forty-eight hours after a tuberculin skin test, the cells were rendered susceptible to lysis by PPD. However, the cells were no more resistant to sonic disruption than were similar cells suspended in normal serum."

AFFRONTI, L. F. **Purified Protein Derivatives (PPD) and Other Antigens prepared from Atypical Acid-Fast Bacilli and** *Nocardia asteroides*. *Amer. Rev. Tuberculosis.* 1959, Mar., v. 79, No. 3, 284–95, 6 figs. [26 refs.]

The atypical acid-fast bacilli from which the antigens were derived were 2 photochromogens from Kansas City and 2 orange-yellow bacilli from the Battey State Hospital, Rome, Georgia, the types of which are not given. The *Nocardia asteroides* was derived from a specimen of sputum. The photochromogens were long slender bacilli that gave a soft, creamy growth, whereas the Battey strains were short bacilli, 1 of which gave a soft tenacious growth and the other a granular growth.

Although the PPD preparations consisted of 93–99% of protein, they contained some carbohydrate, for which there was evidence that some of it was similar to the polysaccharide I and II of the tubercle bacillus. The PPD also contained variable quantities of nucleic acid; the photochromogens contained 0·5 and 0·9%, the Battey strains 0·9 and 2·1%, and the nocardia 0·05%. Deoxyribonucleic acid was present in each of the samples but most of the nucleic acid of the nocardia PPD was ribonucleic acid.

Cross precipitin reactions and agar-gel diffusion tests, with sera from rabbits immunized with the various bacilli, showed that all the PPD samples from the mycobacteria, including PPD from tubercle bacilli, thus shared common antigens; but the PPD from the atypical acid-fast bacilli could be differentiated in the precipitin tests by using high dilutions. The agar-diffusion method showed that these bacilli shared 2 or 3 antigens with BCG. PPD from the photochromogens gave almost identical precipitin bands and the Battey strains showed similar bands but also additional ones. There was no cross-reaction with the nocardia antigen.

In skin reactions in rabbits immunized with the bacilli, all the samples of PPD showed specificity in that the reactions were strongest with the homologous antigen. Similarly, although the rabbit immunized with BCG reacted to all the antigens, including that from the nocardia, it reacted most strongly to the PPD from the tubercle bacillus. Cross-sensitization was also seen in the guineapig sensitized with human tubercle bacilli, but the strongest reaction was again seen with the homologous PPD. *S. R. M. Bushby*

DE SOUZA-ARAUJO, H. C. **The Morphology of** *Mycobacterium leprae*. *Leprosy Review.* 1959, Apr., v. 30, No. 2, 80–84, 31 figs. on 4 pls.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 840.]

U.S. PUB. HEALTH SERVICE—Communicable Dis. Center & NAT. ACAD. SCI.—Nat. Res. Council. **Proceedings of the National Conference on Hospital-Acquired Staphylococcal Disease,** held at Atlanta, Georgia — September 15–17, 1958. pp. xi + 178 + xxxv, illustrated. [Numerous refs.] 1958, Oct. Atlanta: U.S. Dept. Health, Education & Welfare, Georgia.

In September 1958 the U.S. Public Health Service, through its Communicable Disease Centre at Atlanta, Georgia, and the National Academy of Sciences sponsored a National Conference on Hospital-Acquired Staphylococcal Disease.

In opening the Conference L. E. BURNEY (Surgeon-General of the U.S.) spoke on *Staphylococcal Disease: A National Problem* (pp. 3–10) stressing the threat implicit in the appearance of staphylococci having drug-resistance and epidemic propensities, and recalled the relatively recent recognition of this threat; he challenged the Conference to produce "marching orders" for a really substantial counter-attack.

R. E. O. WILLIAMS presented a paper on *Investigations of Hospital-Acquired Staphylococcal Infection and its Control in Great Britain* (pp. 11–29) which was also published under a slightly different title in *Public Health Reports* [see this *Bulletin*, 1959, v. 34, 518].

R. J. ANDERSON (*The Emergence of the Hospital-Acquired Staphylococcal Disease Problem in the U.S.*, pp. 30–38) stressed the problems of collection and communication of information, both within hospitals and between hospitals and public health agencies.

V. KNIGHT, A. WHITE and T. HEMMERLY, studying *The Effect of Antibiotics on Staphylococci of Hospital Patients* (pp. 39–54) had found that antibiotic treatment of hospital patients led to the replacement, in the carriers, of drug-sensitive staphylococci by resistant strains, provided the ward contained a reservoir of such strains, but had little effect on non-carriers, who rarely became carriers. M. LEPPER, in discussion (pp. 55–59) concluded that neither rotation of antibiotics nor the use of combinations of drugs would be nearly so valuable as restriction of the use of the drugs.

T. E. SHAFFER (*Staphylococcal Infections in Newborn Nurseries*, pp. 60–68) reported that all of 70 outbreaks of infection in various parts of the world from which he had examined staphylococci had proved to be due to a single type [80/81]. He had been impressed by the frequency with which personnel in a hospital became carriers and thought that infection might be controlled by excluding carriers of notorious types of staphylococci from the nursery. He had also succeeded in controlling colonization of infants by bathing them with hexachlorophene. In the discussion, R. T. RAVENHOLT (pp. 69–74) emphasized the need for surveillance to establish the incidence of disease, *e.g.* by telephone survey (details of the method are given as an appendix) and pleaded for more room for isolation of infants, improved nursery hygiene and reduction of the skin carrier load of staphylococci among the staff by daily showers and washing with antiseptic soap before starting work.

C. W. HOWE summarized his experience of *Staphylococcal Disease on Surgical Services* (pp. 75–92), giving figures for the prevalence of sepsis in clean wounds over a 9-year period, with a rise from 1% to 4% between 1949 and 1953, and a downward trend subsequently. He thought most of the serious infections were contracted in the operating room, and, in addition to aseptic measures, stressed the need for meticulous surgical technique if sepsis is to be avoided. H. T. CASWELL (Discussion pp. 93–97) also thought that operation room infection was the most important and called for improvements both in surgical and aseptic technique, and in operation room behaviour.

D. E. ROGERS and I. L. BENNETT describing *Staphylococcal Disease on General Medical Services* (pp. 98–104) claimed that, although the staphylococcal infections observed are predominantly hospital-acquired, they differ from the surgical and maternity unit infections in being sporadic rather than epidemic and they supervene on existing disease. Mortality was a bad index of the magnitude of the problem: in 9 months only 5 of 2,000 patients died from staphylococcal infection, but in the same period 100 non-fatal infections led to an average excess stay in hospital of 11–12 days.

F. H. WENTWORTH, Adah MILLER and Bertina B. WENTWORTH, discussing the *Community Aspects of Hospital-Acquired Staphylococcal Disease* (pp. 105–11), remarked that hospital epidemics may go undetected unless the hospital-acquired disease occurring after discharge is promptly found and brought to the attention of the hospital.

J. E. BLAIR gave a simple account of *Laboratory Aspects of the Problem of Hospital-Acquired Staphylococcal Disease* (pp. 112–22) in which he discussed methods of isolation and identification, including phage typing. The same topic is also presented in the form of detailed instructions in a useful Appendix, *Recommended Procedures for Laboratory Investigation of Hospital-Acquired Staphylococcal Infections*, prepared by J. E. BLAIR, E. K. BORMAN, E. T. BYNOE, E. L. UPDYKE and R. E. O. WILLIAMS. It is recommended that phage typing should only be undertaken by hospitals carrying out special research projects; facilities for typing are being arranged through State Health Laboratories. Interpretation of phage typing results is discussed.

J. C. COLBECK, in a paper on *The Use of the Laboratory in the Epidemiology of Staphylococcal Disease* (pp. 123–33), described investigations on the degree of environmental contamination around patients with staphylococcal infection.

Finally D. A. CLARK presented an important short paper on *Staphylococcal Infection from the Standpoint of the Hospital Administrator* (pp. 134–7), stressing the need to accept responsibility and to take the initiative in coordinating the work of all departments of the hospital.

The Conference included 2 closed discussion sessions which are reported in the form of *Summaries and Recommendations* (pp. 141–58).

Hospital infection committees ought to be set up to collect data on the incidence of infection, to guide control measures, and to educate staff. Information often needs to be transferred between hospitals and to the local health authority. Statutory notification of staphylococcal infection has been introduced in some States.

Some patients are especially susceptible to staphylococcal infection and may be better treated at home rather than in hospital.

All infected patients ought to be nursed in isolation. Any procedure that breaks the skin-barrier, even if only for venesection, offers a portal of entry for the staphylococci and should be done with strict asepsis. Indiscriminate antibiotic therapy was condemned and prophylactic antibiotic therapy considered of use only in maternity nurseries and then as a temporary measure during an epidemic.

Great care needs to be taken with all aspects of hospital " housekeeping ".

All hospital personnel with frank staphylococcal lesions should be excluded from duty and should not suffer financial loss. Only during an epidemic is it necessary to seek inapparent carriers and this search need take account only of strains of the epidemic type. There is a guarded suggestion that routine examination of nursery staff for carriers of notorious types may be useful.

Maternity units ought to set up special surveys to detect infection developing after the infants' discharge from hospital.

Bacteriological services of high calibre need to be available to all hospitals and facilities must be provided for type identification of the staphylococci.

A final Summary of the Conference was presented by H. F. DOWLING (pp. 173–8), who stressed that while many potential paths of infection are known, their relative importance is unknown; and that we still know far too little of *why* particular staphylococci behave in the way they do, and why only *some* of our patients suffer the infections. He closed, in verse, with a plea for more research. *R. E. O. Williams*

STROMINGER, J. L. & THRENN, R. H. **The Optical Configuration of the Alanine Residues in a Uridine Nucleotide and in the Cell Wall of** *Staphylococcus aureus. Biochim. et Biophys. Acta.* 1959, May, v. 33, No. 1, 280–81.

BUTLER, L. O. **Studies on the Preparation and Isoelectric Point of Staphylococcal α-Haemolysin.** *Biochem. J.* 1959, Jan., v. 71, No. 1, 67–73, 4 figs. [13 refs.]

Attempts were made to purify the staphylococcal α-haemolysin produced by growth in a modified Walbum medium, with the use of ammonium sulphate, ethanol and Cellosolve (2-methoxyethanol). None of the 3 methods was completely satisfactory, though the Cellosolve gave material with the highest activity.

The iso-electric point of the partially purified haemolysin was estimated, from examination of its behaviour in the Tiselius apparatus at various *p*H values, as *p*H 6·4; this differed markedly from the value obtained by paper electrophoresis, presumably because of adsorption of the toxin to the paper.

Some evidence was obtained for differential denaturation of the haemolytic and lethal factors in the toxin.

*R. E. O. Willams*

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HLAVA, H. & MARSÁLEK, E. Příspěvek k patogenitě stafylokoků. [**A Contribution towards the Pathogenicity of Staphylococci**] *Českoslov. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 3, 189–96. [29 refs.]

The English summary appended to the paper is as follows:—

"In 121 coagulase-positive staphylococci of an infectious origin and in 60 strains isolated from healthy carriers, the authors investigated the production of alpha toxin, leucocidin, the hemolysis on agar dishes, the clumping factor, fibrinolysin and lecithinase.

"Staphylococci of an infectious origin produce in 90 p. c. alpha toxin as well as leucocidin in high titres, the remaining 10 p. c. produce only one of them. We could not prove in any case a weakly toxic strain.

"Staphylococci isolated from healthy carriers produce great quantities of both of the toxins in 32 p. c. of cases. In 35 p. c. of the strains, a very low production of the toxins could be observed.

"We did not observe any connection between the toxicity of staphylococci and the clinical course of the disease.

"Hemolysis on a standard blood dish may serve, even if for orientation only, as a relatively good indicator of the production of toxins.

"In primoculture, we observed colonies with different hemolytic effect and differing also in the production of alpha toxin.

"The clumping factor, fibrinolysin and lecithinase [are not usually] positive [parallel] with the production of the toxins."

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JELJASZEWICZ, J. Badania nad koagulazami gronkowcowymi. I. Metody oznaczania wolnej i związanej koagulazy. [**Some Experiments in Staphylocoagulase. I. Methods of Determination of Free and Bound Coagulase**] *Acta Microbiologica Polonica.* 1958, v. 7, No. 1, 17–33. [Numerous refs.] English summary.

An investigation of the optimum conditions for carrying out the coagulase test has been made on 500 strains of *Staphylococcus pyogenes.* A greater proportion of positive results was obtained in tube tests by diluting the plasma with broth, and by using rabbit instead of human plasma. In plate tests good results were obtained with agar containing 15–20% of human plasma, even when plasma containing coagulase inhibitors was used, and also with lyophilized human and rabbit plasma. In an examination of samples of plasma from 120 blood donors 60 were found to be suitable for carrying out coagulase tests, the remainder being unsatisfactory on account of lack of activator or excess of inhibitor. In an examination of 100 strains for the presence of bound coagulase, slide and tube tests with human and rabbit plasma and fibrinogen gave essentially the same percentage (70–73%) of positive results.

*D. J. Bauer*

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LIDWELL, O. M. **Apparatus for Phage-Typing of** ***Staphylococcus aureus.*** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, Mar., v. 18, 49–52, 3 pls. & 1 fig.

An apparatus is described for simultaneously applying 27 drops of bacteriophage filtrate to a *Staphylococcus* typing plate. 2 sets of loops at either end of a metal plate are each similar to that described by TARR [this *Bulletin*, 1958, v. 33, 698]. The plate is mounted on a vertical pillar and can be rotated through 4 positions and depressed by means of a lever.

Position 1. The loops are sterilized by a gas burner with 27 jets.

Position 2. They are cooled in tubes blowing unsterile air.

Position 3. They are lowered into the phage filtrates distributed in a drilled Perspex block.

Position 4. The charged loops are lowered onto the surface of a plate previously flooded with the strain to be typed.

Scale diagrams are included and the apparatus is not difficult to make.

A rack of 5 sliding trays is also described to reduce the amount of space needed to type the large number of strains which this apparatus makes possible. [The abstracter has used this apparatus for over a year and finds that the speed of the operation can be further increased by dipping the loops, after applying the phage, in an alcohol bath placed in position 4 underneath the plate being typed. This washes them and decreases the time for flaming and cooling.]

*M. Patricia Jevons*

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ZAK, Cecylia. Adsorpcja bakteriofagów gronkowcowych na filtrach bakteriologicznych. [**Adsorption of Staphylococcal Bacteriophages on Bacteriological Filters**] *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 1, 39–42.

The English summary appended to the paper is as follows:—

"Suspension of three staphylococcal phages at pH—7.0 and pH—8.0 used for typing of staphylococci were filtered through Berkefeld, Seitz and membrane filters. Independently of the kind of filters used higher losses were observed at pH—7.0 than at pH—8.0.

"Seitz filters are unsuitable since they caused losses reaching 90%. Membrane filters were found most suitable. The highest losses observed for membrane filters at pH—8 do not exceed 23%."

KIENITZ, M. & PREUNER, R. Über den Nachweis des Staphylokokken-Enterotoxins. 3. Untersuchungen über die Wirkung des Staphylokokken-Enterotoxins auf Hühnerembryonen. **[On the Demonstration of *Staphylococcus* Enterotoxin. III. Investigations on the Action of *Staphylococcus* Enterotoxin on Chick Embryos]** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 1/2, 56–70. [60 refs.]

Staphylococcal culture filtrates were injected, in doses of 0·05–0·2 ml., into embryonated hens' eggs. Filtrates of strains known, from their past history, to produce enterotoxin commonly killed the embryo in 1–4 days. That the lethal effect was not due to the haemolysin is indicated by the facts that heating of the filtrate destroyed its haemolytic activity without affecting its lethal effect for the embryo and that a staphylococcus antitoxin failed to protect the embryos. Of 42 strains of staphylococci from wound infection etc. only 4 killed 3 or more of the 6 embryos tested.

[No direct comparison with any other method of testing for enterotoxin is reported.]

*R. E. O. Williams*

JACKSON, J. R., GIBBONS, R. J. & MAGNER, D. **The Effects of Staphylococcal Toxin on the Lungs of Rabbits.** *Amer. J. Path.* 1958, Nov.–Dec., v. 34, No. 6, 1051–67, 10 figs. on 3 pls. [22 refs.]

Bacteria-free culture filtrates of the Wood strain of *Staphylococcus aureus*, containing $\alpha$-toxin, were injected intratracheally or intrabronchially into rabbits. The animals were examined, after sacrifice or spontaneous death, at intervals up to 7 days. In the first few hours the only changes were injection of the tracheal mucosa, with frothy exudate, and some areas of red jelly-like consolidation. Later, large peribronchial areas of haemorrhagic congestion developed and proceeded to necrosis. Intravascular injection of trypan blue suggested that damage to blood vessels led to ischaemia of large areas of lung. The picture is considered similar to that seen in early human cases of staphylococcal pneumonia. *R. E. O. Williams*

GRÜN, L. Über Beziehungen zwischen Pigmentation, Antibiogramm und Antigenstruktur bei pathogenen Staphylokokken. **[The Relations of Pigment Production, Resistance to Antibiotics and Antigen Structure in Pathogenic Staphylococci]** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 3/4, 184–91. [13 refs.]

Of 635 strains of coagulase-positive staphylococci, 485 produced a golden pigment and 150 a white pigment. The white-pigmented strains were rather more often penicillin-sensitive than the golden. They were also much more often non- or spontaneously agglutinable with typing sera. Strains with the serological formula *abe* were less often penicillin-resistant than those of the other common types. *R. E. O. Williams*

FISCHER, H. G. Die Häufigkeit penicillinresistenter Staphylokokken. **[The Incidence of Penicillin-Resistant Staphylococci]** *Deut. med. Woch.* 1959, Feb. 13, v. 84, No. 7, 257–8, 287. [15 refs.]

Of 410 " haemolytic " staphylococci from pathological material from 2 hospitals in Kiel, about 55% were resistant to penicillin, about 51% to streptomycin, 16% to tetracycline and 3% to chloramphenicol. Slightly lower rates were observed in 61 strains from private clinics. Only 25% of 63 strains from general practitioners were resistant to penicillin and 17% to streptomycin. *R. E. O. Williams*

COLLARD, P. & HARRIS, W. **A Study of the Antibiotic Sensitivity of *Staphylococcus pyogenes* in an Urban Nigerian Community. With a Note on the Relationship of Penicillin Resistance to Penicillinase Activity.** *West African Med. J.* 1959, Feb., v. 8 (n.s.), No. 1, 28–36, 6 figs. [15 refs.]

200 staphylococci from out-patients and 41 from in-patients in Ibadan between July and December 1956 were examined for their sensitivity to penicillin, streptomycin, chloramphenicol and aureomycin by plate and tube methods. Estimations of penicillinase activity were made on all strains resistant to 1 unit penicillin/ml.

74·5% out-patient strains and 24·4% in-patient strains were sensitive to all antibiotics. 20·5% out-patient strains and 70·7% in-patient strains were resistant to penicillin. These figures are similar to the figures reported for London [BARBER and BURSTON, this *Bulletin*, 1956, v. 31, 206] and may be due to the lack of control of the use and sale of penicillin in Ibadan. There were no significant differences between in-patient and out-patient strains in their resistance patterns to other antibiotics. *M. Patricia Jevons*

SPITZBART, H. Zur Frage der Antibiotika- und Sulfonamidresistenz einschliesslich der biochemischen Leistung bei Mastitiskeimen. **[Resistance to Antibiotics and Sulphonamides and the Biochemical Reactions of Organisms Causing Mastitis]** *Ztschr. f. ärztl. Fortbildung.* 1959, Feb. 1, v. 53, No. 3, 172–7, 5 figs. [Numerous refs.]

The author reviews the literature on puerperal mastitis with reference to its causation and particularly its treatment: this section of the paper abounds in proprietary German names for anti-bacterial drugs. His own observations are based on the examination of 103 specimens of pus and 192 of milk from cases of mastitis: all the former and 158 of the latter yielded a growth of *Staphylococcus aureus*, while 18 and 181 specimens respectively yielded *Staph. albus*. 169 strains of *Staph. aureus* were tested for sensitivity to antibiotics: almost all were resistant to penicillin, about one-half to streptomycin, but less than one-quarter were resistant to chlornitrin (chloramphenicol) and to oxytetracycline and this resistance was all of moderate degree [how the intermediate category into which all these strains fell was defined is not explained: it is surprising that no strains were fully resistant to oxytetracycline].

Tests were also done with 4 sulphonamides, and the great majority of strains were resistant to all of them. In some patients cultures were made from the milk of both breasts, and staphylococci of different antibiotic resistance patterns were usually found on the affected and normal sides. Although *Staph. albus* is considered to play only a small part in producing mastitis 87 strains of this organism were submitted to the same series of sensitivity tests and the results are given. Criteria of pathogenicity in staphylococci are discussed: although the coagulase test is mentioned in the text, it was not one of the 4 tests to which a series of strains of both species was submitted [the usual view is that it renders such tests as mannite fermentation and gelatin liquefaction superfluous.] *L. P. Garrod*

IMSENECKI, A. A., PEROVA, K. Z., ZAIZEVA, T. A. & BELOSERSKY, A. N. [**Transmission of Streptomycin Resistance (Transformation) in Staphylococci by means of DNA**] *Mikrobiologiya.* Moscow. 1959, v. 28, No. 2, 187–90, 4 figs. on pl. [In Russian.]

The English summary appended to the paper is as follows:—

" 1. A streptomycin resistant variant has been obtained by subculturing Staphylococcus aureus 209 to a streptomycin containing medium. DNA has been isolated from the cells of the streptomycin resistant culture.

" 2. Among the non-resistant staphylococci cultivated on a DNA containing nutrient medium some mutants have arisen which grew well on a solid streptomycin containing medium.

" 3. With increase in the DNA content of the medium from 1 $\gamma$ to 5 $\gamma$ per 1 *ml* the number of mutations increased 10 times.

" 4. In the initial non-adapted culture resistant staphylococci are extremely rare, *viz.* one mutation per 1 milliard cells on the average. DNA increases the mutation frequently by 4 thousand times in that at a DNA concentration of 5 $\gamma/ml$ one mutation arises per 250 thousand cells, on the average.

" 5. The effect of DNA is specific since DNA isolated from thymus or from the cells on the non-adapted staphylococcus strain does not cause any transformation."

BECKETT, A. H., VAHORA, A. A. & ROBINSON, Ann E. **The Interaction of Chelating Agents with Bacteria. Part I. 8-Hydroxyquinoline (Oxine) and** *Staphylococcus aureus.* *J. Pharmacy & Pharmacol.* London. 1958, Dec., v. 10, Suppl., 160T–169T, 3 figs. [13 refs.] Discussion 169T–170T.

" The interaction of solutions containing oxine or iron or both (in a 1 : 1 molar ratio) with *Staph. aureus* is examined with respect to the chelating agent and metal ion binding by the bacteria. Iron enhances the amount of oxine uptake by the organism although the presence of the chelating agent does not affect the amount of iron bound. Iron is shown to be present in the ferric state in dilute solutions containing oxine. Two types of iron receptor sites in the bacterial surface are postulated and iron is shown to mediate oxine binding by the bacteria."

RICHOU, R. & RICHOU, R. (Mme.) Influence de l'acide pantothénique sur la production de l'antitoxine staphylococcique chez le lapin. [**Influence of Pantothenic Acid on the Production of Staphylococcal Antitoxin in Rabbits**] *C.R. Soc. Biol.* 1959, v. 153, No. 1, 67–8.

Pantothenic acid played no part as an adjuvant or stimulant of immunity.

JANOVICS, A. **Experimental Immunization of Rabbits with** *Staphylococcus* **Toxoid by the Oral and Nasal Routes.** *South African J. Lab. & Clin. Med.* 1958, Dec., v. 4, No. 4, 262–72. [23 refs.]

Rabbits were given repeated doses of a concentrated staphylococcal toxoid, prepared by formaldehyde treatment of a toxic culture filtrate and subsequent precipitation with ammonium sulphate, potassium aluminium sulphate or trichloracetic acid. The rabbit's sera were tested for antitoxin before and during the immunization course. The best response was obtained from intranasal administration of toxoid, with the oral route almost as good. Intragastric administration produced little effect. Alum-precipitated toxoid was less satisfactory than toxoid solution. The best response yielded a maximum serum titre of 30–40 units per ml. There was often a drop in titre when the serum was tested 30–60 days after immunization. [No comparative tests with intravenous inoculations are reported.]

[In order to make sense the pages of this paper in this issue have to be read in the following order: 262–265, 270, 271, 268, 269, 266, 267, 272.] *R. E. O. Williams*

HAKIM, A. A. **Enzymically Active Proteins from Streptococcal Cells: I. Fractionation and Specificity.** *Enzymologia.* The Hague. 1958, Nov. 15, v. 20, No. 2, 67–85, 6 figs. (3 on 4 pls.) [17 refs.]

Washed deposits of group A, B, C and G streptococci were extracted in various ways and fractions containing M protein, ribonuclease [RNase], deoxyribonuclease [DNase] streptococcal proteinase and diphosphopyridine nucleotidase were prepared by ammonium sulphate and low-temperature ethanol precipitation. The properties of these proteins were studied by paper chromatography, paper electrophoresis and spectrophotometry.

Hot-acid extracts of the deposits were examined for M protein by precipitation reactions with immune sera [the choice of group M type 4 cells for many of the experiments is unfortunate as the M protein of this type is poorly developed, not typical and good type specific antiserum is notoriously difficult to prepare]. Spectrophotometry of these fractions indicated that the

M antigen was associated with large amounts of nucleic acid which resisted removal by DNase and RNase. The interaction of this material with nicotinic acid and its derivatives was also studied.

Cellular ribonuclease was found in free and combined forms; the latter was activated 100-fold by 0·25 M sulphuric acid and both acid and alkaline ribonuclease activities were found in the cells. In general the former were thermolabile and the latter thermostable, both destroyed yeast RNA. Deoxyribonuclease activity was found to be both cellular and extracellular, the cellular material contained fractions with neutral and alkaline optimal *p*H activities. The ability to destroy or combine with diphosphopyridine nucleotide [DPN] was widely distributed throughout the prepared fractions. The streptococcal proteinase was shown to destroy the M protein *in vitro*. [All these fractions appear to be complex mixtures and conclusions drawn from the results must be interpreted with caution.]

*M. Patricia Jevons*

PALVA, I. P. & KAIPAINEN, W. J. **Sensitivities of Beta-Haemolytic Streptococci. Follow-Up Studies with Scarlet Fever Patients treated with DBED-Penicillin or Tetracycline.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1959, v. 37, No. 1, 1–8.

Of a series of 200 patients with scarlet fever, 100 were treated with benzathine penicillin (300,000 units together with 150,000 units each of procaine and potassium penicillin, followed by 1,200,000 units of benzathine penicillin alone after 6 and 20 days) and 100 with tetracycline (either 12 or 25 mgm./kgm. body weight for 5 days). Throat cultures, 6 or 20 days or both after treatment was started, yielded haemolytic streptococci (almost always of the same serological type as those originally found) in only 6 penicillin-treated cases and in 32 treated with tetracycline. The sensitivity of the streptococci to the antibiotic used remained unchanged in all cases: all were inhibited by 0·05 unit/ml. or less of penicillin, but the minimum inhibitory concentration of tetracycline varied from 0·4 to 6 μgm./ml.; *i.e.* some of them were abnormally resistant before treatment started. There is some discussion of whether the doses used can produce adequate therapeutic concentrations of the antibiotic in the blood and in the substance of the tonsil.

*L. P. Garrod*

JACKSON, S., MACLEOD, C. M. & KRAUSS, Marjorie R. **Determination of Type in Capsulated Transformants of Pneumococcus by the Genome of Non-Capsulated Donor and Recipient Strains.** *J. Exper. Med.* 1959, May 1, v. 109, No. 5, 429–38.

PERELLI, C. "Formazioni L" di *Diplococcus pneumoniae.* [**L Forms of** *Diplococcus pneumoniae*] *Igiene Moderna.* 1958, Nov.–Dec., v. 51, Nos. 11/12, 895–902, 8 figs.

The English summary appended to the paper is as follows:—

"The morphologic aspects of "L formations" which developed from an expectoration sample and later gave rise to the growth of Diplococcus pneumoniae have been studied."

LEÓN, A. P. & CANO, Carmen. Antigeno artificial anti-*Brucella* preparado con un polisacárido aislado de *Brucella melitensis* por biodiálisis. Sus propiedades inmunológicas. [**Artificial Antigen Prepared from Polysaccharides Extracted from** *Br. melitensis.* **Its Immunological Properties**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1958, June, v. 18, No. 2, 45–61. [21 refs.] English summary (8 lines).

By extraction of washed suspensions of *Br. melitensis* at various temperatures with sterile distilled water, the period of extraction being longer at lower temperatures, the authors obtained supernatants from which matter precipitable by 96% alcohol in presence of 3% Na acetate could be obtained and the precipitate so purified that ultimately its solutions give the Molisch but not the biuret or xanthroprotein reactions. This material was assumed to be polysaccharide and behaved like a hapten, reacting with antibrucella sera in high dilutions 1 to $10^6$ and not functioning as antigen.

When, however, large molecular aggregates were obtained by treatment with aluminium phosphate, the product could be shown to evoke precipitating and complement-fixing antibodies in the animals injected and to render them more resistant to lethal injections of *Brucella* suspension. The opsonic cytophagocytic index of the rabbits and goats injected was also observed to be raised.

No allergic skin reactions were observed in animals sensitized with the preparation however.

*J. W. McLeod*

TUSKIEWICZ, Maria. **Investigations on Incomplete Antibodies during** *Brucella* **Infections** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Apr., v. 117, No. 4, 281–4. [13 refs.]

The English summary appended to the paper is as follows:—

"The performing of blocking and Coombs test in Brucella infection is necessary if the Wright test is negative.

"The blocking and incomplete antibodies show a great specificity. This problem of great importance should be further elaborated."

OLITZKI, A. L. & GODINGER, D. **Influence of Pentoses on the Oxygen Uptake of Haemophilus Strains.** *J. Bacteriology.* 1958, Aug., v. 76, No. 2, 160–2, 2 figs.

*Haemophilus aegyptius* strains showed high endogenous respiratory rates which were either unchanged or lowered in the presence of 1% xylose. Some strains, however, utilized ribose. *H. influenzae* strains showed relatively low endogenous respiratory rates which were enhanced in the presence of xylose. There was a strain difference, however, in their ability to utilize ribose and arabinose.

The majority of *H. aegyptius* strains agglutinated red blood cells (RBC) from different species (man, mouse, guineapig) whereas *H. influenzae* strains did not agglutinate RBC from the mouse and guineapig and gave only weak reactions with human RBC.

An intermediate strain (9591) has been isolated from patients with conjunctivitis in Israel which is xylose positive and agglutinates RBC from all 3 animal species.

*F. T. Perkins*

Vainer, Henriette, Faur, Yvonne, Tigoiu, Viorica & Ionesco, Honorina. Recherches sur la préparation du vaccin *H. pertussis.* **[Studies on the Preparation of** *Haemophilus pertussis* **Vaccine]** I-er mémoire. *Arch. Roumaines Path. Expér. et Microbiol.* 1957, Dec., v. 16, No. 4, 593–608, 6 graphs & 4 diagrams. [38 refs.]

The authors have prepared pertussis vaccines from organisms grown on a semi-synthetic solid medium similar to that of Cohen and Wheeler [this *Bulletin*, 1947, v. 22, 558]. The medium (SSS) contains casein hydrolysate, cystine and tryptophan, inorganic salts, yeast extract and nicotinic acid, activated charcoal or aluminium silicate and amidon. This medium, which is solidified with agar, supports the growth of phase I *Haemophilus pertussis* and vaccines prepared from the organisms have greater immunological activity than those prepared from organisms grown on the classical blood agar medium.

The authors consider that the measurement of dry weight of organisms/ml. in the vaccine is a better way of standardization than the usual method of turbidity measurements.

*F. T. Perkins*

Kind, L. S. **The Altered Reactivity of Mice after Inoculation with** *Bordetella pertussis* **Vaccine.** *Bact. Reviews.* 1958, Sept., v. 22, No. 3, 173–82. [80 refs.]

Inoculation with a single dose of *Bordetella* [*Haemophilus*] *pertussis* organisms increases the sensitivity of mice to the lethal effects of histamine, serotonin, anaphylaxis and Gram-negative bacterial vaccines as well as to physical conditions of reduced atmospheric pressure, cold stress and irradiations.

The author has given a comprehensive account of the findings of the many workers studying the conditions necessary to effect the increased sensitivities.

In his hypothesis an attempt has been made to correlate these findings. Present investigations are based on 2 assumptions (a) sensitivity to histamine, serotonin, anaphylaxis, endotoxins, etc. is due to a defect in steroid metabolism and (b) increased susceptibility to the lethal effects of endotoxins, anaphylaxis, peptones, etc. is due to the release of histamine or serotonin or both in an animal somehow made sensitive to histamine and serotonin. The first assumption may be proved or disproved in the near future whereas clarification of the second assumption will depend upon a better understanding of the complex interrelationship between histamine, serotonin, epinephrine and acetylcholine. In this respect studies on mast cells will be most interesting.

*F. T. Perkins*

Kovaleva, R. V. **Certain Characteristics of** *Pasteurella pestis* **Strains isolated in Mongolia from** *Microtus brandti* **and other Rodents.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 8, 1205–13, 4 figs. [11 refs.] [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 826.]

Delwiche, E. A., Fukui, G. M., Andrews, A. W. & Surgalla, M. J. **Environmental Conditions affecting the Population Dynamics and the Retention of Virulence of** *Pasteurella pestis*: **the Role of Carbon Dioxide.** *J. Bacteriology.* 1959, Mar., v. 77, No. 3, 355–60, 2 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 824.]

Higuchi, K., Kupferberg, L. L. & Smith, J. L. **Studies on the Nutrition and Physiology of** *Pasteurella pestis.* **III. Effects of Calcium Ions on the Growth of Virulent and Avirulent Strains of** *Pasteurella pestis. J. Bacteriology.* 1959, Mar., v. 77, No. 3, 317–21, 1 fig. [11 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 825.]

Anisimov, P. I. **Cytology of** *Pasteurella pestis* **in the Process of Variation.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 8, 1200–205, 4 figs. [14 refs.] [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 825.]

Chmura, N. W. & Pelczar, M. J. **Enhancement of Pseudomonad Pigment Production by** *Serratia marcescens. J. Bacteriology.* 1959, Apr., v. 77, No. 4, 518–9, 1 fig.

Thayer, J. D., Field, Frances W. & Garson, W. *In vitro* **Susceptibility of** *Neisseria gonorrhoeae* **to the Action of Sulfamethoxypyridazine (Kynex) and Sulfadiazine.** *Antibiotics & Chemotherapy.* New York. 1959, Mar., v. 9, No. 3, 176–9.

Gonococci began to show sulphonamide resistance in 1940 and by 1948 only 16% of strains tested in one study were inhibited by sulphadiazine (100 $\mu$gm./ml.); in 1954, however, it was found that 89% of strains tested were susceptible to this concentration.

These authors carried out tests on sulphadiazine and on sulphamethoxypyridazine adding varying amounts to culture medium inoculated with gonococci; results are set out in 2 tables.

The average minimal inhibitory concentrations after 24, 48 and 72 hours for sulphamethoxypyridazine were 24, 46 and 54 $\mu$gm./ml. and for sulphadiazine 17, 38 and 43 $\mu$gm./ml.

These figures refer to gonococci isolated in North Carolina but are similar to those obtained in Boston; it is calculated that blood levels sufficient to inhibit 95% of gonococci could be attained but it has not been proved that this would be effective *in vivo*.

*T. E. Osmond*

DOAK, G. O., FREEDMAN, L. D. & CLARK, J. W., Jr. **Ionic Requirements of** *Treponema pallidum*. **I. Sodium and Potassium.** *J. Bacteriology.* 1959, Mar., v. 77, No. 3, 322–7. [15 refs.]

" Sodium chloride in physiological concentration is toxic to *Treponema pallidum*. The concentration of sodium ion for optimal survival *in vitro* is approximately 0.029 M. The minimal concentration of potassium ion for optimal survival *in vitro* is approximately 0·01 M. Higher concentrations of potassium ion are not toxic. Moderately hypotonic or hypertonic solutions are not inferior to isotonic solutions for the survival of *T. pallidum*."

MYERSON, R. M., WOLFSON, S. W. & SALL, T. **Preliminary Observations on the Cultivation and Morphology of a Microorganism from the Cerebrospinal Fluid of Patients with Multiple Sclerosis.** *Amer. J. Med. Sci.* 1958, Dec., v. 236, No. 6, 677–91, 15 figs. [47 refs.]

A micro-organism described as a motile spirochaete was obtained in cultures from cerebrospinal fluid of 5 out of 13 patients with multiple sclerosis.

All of 21 observations in cases of other nature were negative.

Details of media used and electron microscope and phase contrast photography of preparations obtained are included.

[See also this *Bulletin*, 1957, v. 32, 1197.]

*J. W. McLeod*

VAN RIEL, J. & VAN RIEL, M. Un procédé simple de coloration des leptospires. **[A Simple Method for Staining Leptospires]** *Ann. Soc. Belge de Méd. Trop.* 1958, Dec. 31, v. 38, No. 6, 1101–2.

The English summary appended to the paper is as follows:—

" Drop 3 drops of culture or suspension of leptospirae in a hemolysis tube, then add 3 drops of May-Grünwald. After 2 minutes add 2 drops of distilled water. After 5–10 minutes put a drop of this mixture on a very clean slide and allow to dry."

BEAM, W. E., Jr. **Effect of Excess Nitrite on Tests for Indole and the Cholera Red Reaction.** *J. Bacteriology.* 1959, Mar., v. 77, No. 3, 328–30.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 829.]

DOMARADSKII, I. V., ANOKHINA, C. V., KULIKOVA, V. L., DENISENKO, L. K. & MOSOLOVA, O. N. **The Use of the Phage Titre Increase Reaction for the Rapid Detection of** *Vibrio comma*. *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 7, 1124–8, 1 fig. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 829.]

LOWENTHAL, J. P. & BERMAN, S. **Ovomucinase Activity in Clostridia.** *J. Bacteriology.* 1959, Apr., v. 77, No. 4, 516–7.

ALEKSANDROWICZ, Janina. Oznaczanie kwasów tłuszczowych od $C_1$ do $C_6$ w hodowlach beztlenowo rosnących zarodnikowców sacharolitycznych. **[$C_1$–$C_6$ Fatty Acids in Cultures of some Saccharolytic** *Clostridia*] *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 1, 19–30, 4 figs. [12 refs.] English summary.

ALBRYCHT, Henryka & TREMBOWLER, Paulina. Wpływ niektórych czynników w podłozu na zarodnikowaine laseczek z grupy *Cl. perfringens*. **[Influence of some Factors present in the Nutrient Media on the Sporulation of** *Clostridium welchii*] *Méd. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 1, 13–18.

The English summary appended to the paper is as follows:—

" *Clostridium perfringens* strains of type A, B, C, D, E, F, were used in this work. Strains were cultivated in the medium of Ellner and in modifications of it. In the last case some constituents of the medium or a number of them were omitted. The growth of cells, the amount of spores in the cultures as well as the thermoresistance of spores were determined. Experiments with cultures on media containing brain tissue were carried out parallelly. The sporulation of all examined *Cl. perfringens* type A strains in the Ellner medium was observed. Some strains of other types of *Cl. perfringens* did not sporulate here or form spores to a very low degree. The presence of starch in the medium has a positive influence on the growth of the vegetative cells mainly, the intensity of sporulation gets stronger only sometimes. Yeast extract doesn't influence either the growth of cells or their sporulation. The phosphates in the Ellner medium stimulate the process of sporulation only. When in the Ellner medium distilled water was substituted by beef heart infusion broth a drop in the number of spores is observed though the growth of bacteria was in both media the same."

JAYKO, L. G. & LICHSTEIN, H. C. **Nutritional Factors concerned with Growth and Lecithinase Production by** *Clostridium perfringens. J. Infect. Dis.* 1959, Mar.–Apr., v. 104, No. 2, 142–51, 4 figs. [11 refs.]

SHELDON, D. R., MOSKOWITZ, M. & DEVERELL, M. W. **Agar Diffusion Procedures for the Assay of Lecithinase from** *Clostridium perfringens. J. Bacteriology.* 1959, Apr., v. 77, No. 4, 375–82, 1 fig. [12 refs.]

MEISEL, H., ALBRYCHT, H. & RYMKIEWICZ, D. **Phospholipase C in Extracts of Mechanically Disintegrated Vegetative Cells and Spores of** *Clostridium perfringens* **Type A and** *Clostridium sordellii. Bull. Acad. Polonaise des Sci.* Warsaw. *Sér. Sci. Biol.* 1959, v. 7, No. 4, 139–42. [15 refs.]

DOLIN, M. I. **Oxidation of Reduced Diphosphopyridine Nucleotide by** *Clostridium perfringens.* **I. Relation of Peroxide to the Over-All Reaction.** *J. Bacteriology.* 1959, Apr., v. 77, No. 4, 383–92, 5 figs. [37 refs.] **II. Purification of the Oxidase; Relation to Cytochrome** *c* **Reductase.** *Ibid.*, 393–402, 8 figs. [21 refs.]

MOUSSA, R. S. **Antigenic Formulae for** *Clostridium septicum* **and** *Clostridium chauvoei. J. Path. & Bact.* 1959, Apr., v. 77, No. 2, 341–50. [47 refs.]

" Examination of 37 strains having in the main the cultural characters of *Clostridium septicum* and 37 strains having those of *Cl. chauvœi* shows:

" (*a*) that *Cl. septicum* strains can be divided into six groups defined by two O and five H antigens;

" (*b*) that all but two *Cl. chauvœi* strains possess a single O antigen, and can be divided into two groups based on two H antigens which, like the single O antigen, are distinct from those of *Cl. septicum*;

" (*c*) that all strains of *Cl. septicum* and *Cl. chauvœi* possess a single common spore (S) antigen;

" (*d*) that the remaining two strains of *Cl. chauvœi* show no antigenic relationship to the other *Cl. chauvœi* strains, but possess antigens occurring in some *Cl. septicum* strains.

" It is suggested that the serological and other differences between *Cl. septicum* and *Cl. chauvœi* do not justify regarding them as two distinct species, and that they might very well be regarded as types A and B of the single species *Clostridium septicum* (Macé 1888, Ford, 1927, both cited by Breed, Murray and Hitchens, 1948)."

PUBLIC HEALTH LAB. SERVICE. **Occurrence of Tetanus Spores in Materials used for Dressing Wounds.** Report of the Public Health Laboratory Service (Medical Research Council, London). *Brit. Med. J.* 1959, May 2, 1150–54. [36 refs.]

This investigation was prompted by a series of cases of post-operative tetanus in which suspicion was thrown upon surgical dressings, among other possible sources of infection. Over 600 samples of dressing materials were examined culturally for *Clostridium tetani*, in 14 Public Health Laboratories. Identification of positive cultures was by biochemical and serological means. Toxicity was tested by controlled animal inoculation.

The results of the survey showed that from 666 samples *Cl. tetani* was isolated on 23 occasions. 20 isolations were from 100 specimens of unbleached cotton wool or cotton-wool bandages, and most of these positive samples were supplied by a single firm. The other 3 isolations were one each from 122 specimens of bleached cotton wool, 145 of gauze, and 12 of stockinet. Negative results were obtained from 51 specimens of cellulose wadding, 15 of paraffin gauze, 21 of plaster bandages, 108 of cotton and crepe bandages, 75 of lint, gamgee, felt and tow, and 17 of dusting powder.

It is concluded that unbleached cotton wool is the form of dressing most likely to be contaminated, and that all dressing materials should be sterilized before use. In view of the potential presence of tetanus spores in unsterilized dressings it is suggested that they should not be allowed into the area of the operating theatre but should be sterilized elsewhere.

The paper includes a most useful and comprehensive review of the literature on this subject.

*J. C. Kelsey*

STRANGE, R. E. **Cell Wall Lysis and the Release of Peptides in** *Bacillus* **Species.** *Bact. Reviews.* 1959, Mar., v. 23, No. 1, 1–7, 2 figs. [39 refs.]

WORK, Elizabeth. **The Action of a Lytic Enzyme from Spores of a** *Bacillus* **on Various Species of Bacteria.** *Ann. Inst. Pasteur.* 1959, Apr., v. 96, No. 4, 468–80, 6 figs. [24 refs.]

The English summary appended to the paper is as follows:—

" 1. A bacteriolytic enzyme was prepared from spores of *Bacillus* sp. 5832; its lytic activity at pH 8.0 was tested against cells of various species of bacteria.

" 2. Washed fresh cell suspensions of *Bacillus* sp. 5832 or *Proteus vulgaris* were lysed slowly by the enzyme; fresh *E. coli, S. typhimurium* and *B. megaterium* were not attacked. Certain preliminary treatments of all these organisms rendered them more susceptible to lysis; either chloroform, acetone, versene, polymixin, or deoxycholate were effective. The enzyme had no action on *Staph. aureus* and *Micrococcus lysodeikticus* under any conditions.

" 3. The enzyme solubilised a peptide component of the walls of *E. coli.*

" 4. The enzyme had no effect on the growth rate of *E. coli* and *S. typhimurium* in glucose-salts media with or without added bile salts and pancreatic enzymes."

STAMATIN, N. Transduction phagique de la sporogenèse chez *B. anthracis.* **[Phage Transduction of Sporogenesis in** *B. anthracis*] *Ann. Inst. Pasteur.* 1959, Apr., v. 96, No. 4, 502–5.

The English summary appended to the paper is as follows:—

"1. By means of the E specific phage, the author succeeded in inducing sporogenesis in several asporogenous *B. anthracis* strains, particularly in recently isolated strains. He never succeeded in inducing sporogenesis in asporogenous strains isolated and kept in the laboratory for more than one year. Besides, all recently isolated asporogenous strains have not the same comportment: some of them e. g. strain 1891, rapidly react to the phage infection by production of asporogenous germs, others are not influenced by the phage.

"2. It seems that the phage, after multiplying in sporogenous germs (and so becoming a carrier of the sporogenesis factor), transfers this factor to the asporogenous germs into which it penetrates. We are here in presence of a phage transduction phenomenon."

## FUNGI

RAUBITSCHEK, E. **Taurocholate Agar for Chlamydospore Production by** *Candida albicans*. *Mycopathologia.* The Hague. 1958, Sept. 29, v. 9, No. 4, 285–7. [10 refs.]

"The taurocholate medium ("tch") consisted of 1% sodium taurocholate c.p., 1.8% agar, in distilled water. After sterilisation 10 to 15 ml. portions of the medium were poured into petri plates and the plates left standing until solidification of the agar. The strains of *Candida* were isolated from skin, nails, nail folds, mucous membranes, sputum, bronchial washings, and stools, on 2% glucose agar with or without the addition of antibiotics. The strains were processed in the usual manner. After two to three days of incubation of the primary isolates the growth was transferred directly to one sector of the tch-agar plate by three short streaks with a needle. Each plate accommodated six-strains. After incubation at 26°C for 24 to 48 hours the unopened plates were put bottom up on the stage of the microscope and the strains examined under low power. Filament formation and abundant chlamydospores could be easily seen at the edges of the streaks. The results of the routine identification procedures were compared with the results of the tch plates.

"Results using a simple medium which encourages rapid formation of chlamydospores in *Candida albicans* and allows the use of contaminated or mixed primary isolates of *Candida* strains are described."

TSUCHIYA, T., FUKAZAWA, Y. & KAWAKITA, S. **A Method for the Rapid Identification of the Genus** *Candida*. *Mycopathologia.* The Hague. 1959, Mar. 31, v. 10, No. 3, 191–206. [22 refs.]

In this paper the authors record the results of serological tests (by the slide-agglutination method with monospecific or absorbed antisera) on a number of strains of *Candida* species supplied from various sources. Identification results obtained by this method compared very favourably with results obtained by already well-established biological techniques such as corn-meal agar culture and fermentation series. In fact, in the case of some strains of *C. albicans* in which it was impossible to obtain chlamydospores in corn-meal agar identification was possible by this serological method. The authors are therefore of the opinion that identification by the serological method which is based on the antigenic structure of species of *Candida*, is a useful, reliable and rapid means of identifying species belonging to this genus. *C. J. La Touche*

LINDH, H. F. **A Method for Evaluation of Anti-Fungal Drugs against Enteric** *Candida albicans* **in Mice.** *Antibiotics & Chemotherapy.* New York. 1959, Apr., v. 9, No. 4, 226–31.

Experiments were carried out, firstly to compare the relative antifungal activity of 3 drugs, namely, nystatin, trichomycin and pimaricin against *Candida albicans in vivo* and *in vitro*, with experimentally infected mice for the tests, and secondly, to ascertain if the antifungal activity of nystatin was exerted enterically (*in vivo*) or only on faecal plates (*in vitro*) prepared from the droppings of these mice. The method of administering the inoculum to the mice consisted in supplying them with fluid Sabouraud medium inoculated with *C. albicans* in lieu of drinking water for a period of 18 hours. The drugs were mixed with ground food pellets and administered in this form for a period extending for 24 hours before the administration of the inoculum fluid to 6 hours after the inoculum fluid was withdrawn. At the conclusion of the course of treatment faecal pellets were tested for viability of *C. albicans*. It was found that nystatin was active at 0·0125% in the diet but not lower, and that trichomycin was active at 0·25% in the diet but not lower, representing equivalent activity to nystatin on an *in vitro* unitage basis. Pimaricin was inactive and non-toxic at 0·05% in the diet which was the highest level tested. The author was satisfied that the antifungal activity shown by nystatin was exerted *in vivo*. *C. J. La Touche*

VISCO, G. Ricerche sulla candidosi sperimentale dell'embrione di pollo. Nota I.—Le caratteristiche generali del processo. [**Researches on Experimental Candidosis of the Chicken Embryo. Note I. The General Characteristics of the Process**] *Riv. Istituto Sieroterap. Ital.* 1959, Jan.–Feb., v. 34, No. 1, 29–46, 2 figs. [18 refs.] English summary.

In studies at the University of Rome of the microbiological aspects of infection experimentally induced in the embryo of the chicken through the allantoid membrane with 21 fungal strains (including 16 of *Candida*) it was ascertained that localized infection by *Candida* species is produced in the allantoid cavity, infection tending to spread somewhat to the embryo and causing a low, irregular rate of mortality among the infected eggs. The embryos were, however, highly susceptible to infections with *Candida* through the yolk sac, dying rapidly when inoculated with *C. albicans* or *C. tropicalis*. Susceptibility was, however, restricted to the first half of the period of pre-natal growth; after the 12th day, a progressively increasing resistance developed, which appeared to persist after the birth of the chick and to result, presumably, in non-apparent infection.

Yolk-sac inoculations with different species of *Candida* gave results agreeing perfectly with those obtained in pathogenicity tests on rabbits and it is suggested that inoculations of chicken embryos should be included among the routine tests used for the identification of *Candida* species. *A. A. Barge*

RODRÍGUEZ, M., J. D. Aislamiento de hongos patogenos del suelo. [**Isolation of Fungi from Soil**] *Rev. Ecuatoriana de Hig. y. Med. Trop.* Guayaquil. 1958, Jan.–Mar./Apr.–June, v. 15, Nos. 1/2, 5–12, 6 figs. English summary (8 lines). [Summary taken from *Rev. Med. & Vet. Mycol.*, 1959, June, v. 3, Pt. 6, 170.]

At the Facultad de Medicina, Universidad de Guayaquil, 7 soil samples from poultry runs, examined by Vanbreuseghem's hair bait method [1, No. 2544], yielded *Trichophyton mentagrophytes* (once) and *Microsporum gypseum* (4 times).

EVOLCEANU, R. & ALTERAS, I. Le *Microsporum gypseum*. Quelques observations cliniques et mycologiques concernant ce dermatophyte. [**Clinical and Mycological Observations on** *Microsporum gypseum*] *Mycopathologia.* The Hague. 1958, Dec. 30, v. 10, No. 2, 71–82, 9 figs. [16 refs.]

VIEU, M. & SEGRETAIN, G. Contribution a l'étude de *Geotrichum* et *Trichosporum* d'origine humaine. [**Contribution to the Study of** *Geotrichum* **and** *Trichosporon* **of Human Origin**] *Ann. Inst. Pasteur.* 1959, Apr., v. 96, No. 4, 421–33, 3 figs. on pl. & 1 text fig. [18 refs.]

The English summary appended to the paper is as follows:—

"From pathological material originating from various sources, arthrospore fungi have been isolated in 7% of the cases. The study of their morphology on potato medium in slide-cultures allows to differentiate *Geotrichum* (which only form arthrospores) from *Trichosporon* (which form arthrospores and blastospores). The physiological properties confirm the results obtained by the study of their morphology. Thirteen *T. cutaneum* and fifteen *G. candidum* have been identified by comparison with fourteen strains originating from various collections.

"The pleomorphic evolution of these strains is discussed."

EVANS, J. H. & BAKER R. D. **Treatment of Experimental Aspergillosis with Amphotericin B.** *Antibiotics & Chemotherapy.* New York. 1959, Apr., v. 9, No. 4, 209–13, 2 figs. [20 refs.]

12 rabbits were treated in the following manner: 4 were used as controls; in 2 treatment commenced two days after inoculation with a spore-suspension of *Aspergillus fumigatus*; in the remaining 6 treatment commenced immediately after inoculation with the spore-suspension. In all cases treatment consisted of a 1 mgm./kgm. intravenous injection daily of a soluble preparation of amphotericin B. Results showed that the untreated rabbits all died in 3 to 4½ days and at autopsy revealed widespread lesions in many of which the fungus was subsequently observed microscopically. However, contrary to expectation, although many lesions were present in the lungs, they did not contain any visible fungus, but instead, clumps of mononuclear cells with some silver-positive débris. The 6 rabbits in which treatment began immediately after inoculation remained apparently unaffected at 4 to 8 days and on being killed did not, at autopsy, reveal any lesions attributable to the fungus. Of the 2 rabbits treated 2 days after inoculation, one was severely infected at 3½ days while the other remained virtually free from infection at 8 days. These therapeutic results are in direct contradistinction to *in vitro* results with amphotericin B when tested against this fungus. Positive cultures for *A. fumigatus* were obtained from all the inoculated rabbits at autopsy. In view of this it is concluded that the therapeutic activity of this drug in this series was fungistatic rather than fungicidal. *C. J. La Touche*

DE MONTEMAYOR, L., HEREDIA OSIO, Blanca & DE BELLARD PIETRI, E. P. Aislamiento del *Histoplasma capsulatum* en el suelo de dos cavernas en Venezuela. Nuevas técnicas de investigación por "Método de Flotación". [**Isolation of** *Histoplasma capsulatum* **in the Soil of Two Caves in Venezuela. A New Technique, the "Flotation Method"**] *Rev. Sanidad y Asistencia Social.* Caracas. 1958, Jan.–Apr., v. 23, Nos. 1/2, 39–54, 2 diagrams & 12 figs. on 5 pls. [29 refs.] English summary.

The English summary appended to the paper is as follows:—

"1. A mycological study was made of earth samples taken from 7 caves in Venezuela. Two methods of study were used to isolate saprophytic and parasitic fungi: Direct method: By direct examination of suspensions of the specimen. A new technique was developed, the 'Flotation Method'. Indirect method. By inoculation of mice.

"2. Histoplasma capsulatum was isolated from earth samples taken from two caves: 'El Peñón' y 'Las Guacas', both by the direct and the indirect method (see plates No. I and II).

"3. The list of all saprophytic fungi found in the earth samples studied is given."

SALVIN, S. B., with the technical assistance of Jane NISHIO. **The Influence of Leucocytes from Sensitized Mice on Resistance to** *Histoplasma capsulatum.* *Amer. J. Hyg.* 1958, Nov., v. 68, No. 3, 233–41, 6 figs. [13 refs.]

"Mice were injected with one of the following antigens: (*a*) live cells of the yeast phase of *Histoplasma capsulatum*, (*b*) killed cells of the yeast phase, (*c*) a cell-wall fraction, and (*d*) a cytoplasmic fraction. Leucocytes were obtained from the buffy coats of each of these groups and injected intraperitoneally into normal recipient mice. Recipient mice that received leucocytes from donor mice injected with live cells, killed whole cells, or the cytoplasmic fraction contained, after challenge with $2 \times 10^6$ cells of *H. capsulatum*, more fungal cells than mice that received leucocytes from normal donors. Recipients of leucocytes from donor mice injected with a cell-wall fraction did not show an increase in fungal cells."

SEELIGER, H. P. R. Das kulturell-biochemische und serologische Verhalten der Cryptococcus-Gruppe. **[Cultural, Biochemical and Serological Reactions of the *Cryptococcus* Group]** *Ergebn. Mikrobiol. Immunitätsf.* 1959, v. 32, 23–72, 8 figs. [204 refs.]

## BACTERIOPHAGES

FRICK, G. & ALBERTSSON, P. Å. **Bacteriophage Enrichment in a Liquid Two-Phase System with Subsequent Treatment with "Freon" 113.** [Correspondence.] *Nature.* 1959, Apr. 11, v. 183, 1070–72, 1 fig. [10 refs.]

The concentration and purification of phage T2 is described. It was calculated from the relation of the distribution co-efficient to molecular size that, in a liquid 2-phase system of the polymers dextran and methyl cellulose, particles of the size of T2 would be 400 times more concentrated in the bottom dextran phase than in the top methyl cellulose phase. In practice, the 2 polymers were mixed thoroughly with a T2 lysate and the mixture left to separate for 48 hours in the cold. The bottom, dextran-rich phase, which was turbid, was drawn off and found to contain about 97% of the phage with a 10-fold increase in titre, the 3% lost remaining in the clear, upper phase.

The concentrated phage was freed from protein by treatment with the fluorocarbon "Freon 113" [sold in Britain by ICI as "Arcton 63"] in a Waring blendor in ice. Dextran had a protective effect on the phage, its titre remaining unchanged or even increasing slightly on shaking with Freon, whereas the same treatment of phage in buffer caused a 1,000-fold drop in titre each time. The removal of protein by treatment with Freon and then dialysis, and the removal of free nucleotides by adsorption with calcium hydroxylapatite, was followed in the UV spectro-photometer.

*Janice Taverne*

WHITFIELD, J. F. & BAIRD, K. M. **Nucleic Acid Synthesis by a Lysogenic Strain of *Escherichia coli* infected with an rII Mutant of Coliphage T2.** *Canadian J. Microbiol.* Ottawa. 1959, Feb., v. 5, No. 1, 17–24, 6 figs. [17 refs.]

Unlike wild type T2, mutants of the r II region of T2 cannot form plaques on *Escherichia coli* lysogenic for λ. It is known that the mutants can adsorb to and kill *E. coli* cells carrying λ prophage, and that phage DNA enters the cell, because, after infection with 2 different r II mutants, recombination occurs yielding normal, wild type, phage. Theoretically, the failure of such a mutant to multiply could result from (1) inability to initiate DNA synthesis, (2) inability to maintain DNA synthesis once initiated or (3) a defect in maturation of phage.

To distinguish between these possibilities, normal and lysogenic cultures of *E. coli* C112, irradiated with UV light and unirradiated, were infected with an r II mutant and DNA and RNA estimated at intervals. (The cells were extracted with hot trichloracetic acid and deoxyribose was estimated by the diphenylamine, and ribose by the orcinol, method.) It was found that net RNA synthesis stopped in all cultures upon infection with the r II mutant. In the lysogenic cells, DNA synthesis was initiated by the mutant, but not maintained. Irradiation of lysogenic cells, and consequent induction of λ, before infection with the mutant did not allow DNA synthesis. The maintenance of DNA synthesis by the T2 mutant appears, therefore, to be inhibited by a mechanism connected with the prophage λ.

*Janice Taverne*

TESSMAN, Ethel S. & TESSMAN, I. **Genetic Recombination in Phage S13.** [Correspondence.] *Virology.* New York. 1959, Apr., v. 7, No. 4, 465–7.

## VIRUSES

*In this section the abstracts are arranged as far as possible in the following order:—General; Psittacosis-lymphogranuloma viruses; Pox viruses; Respiratory and other viruses; Enteric viruses; Arthropod-borne viruses; Others.*

UNDERWOOD, G. E., SIEM, R. A., GERPHEIDE, Shirley A. & HUNTER, J. H. **Binding of an Antiviral Agent (Kethoxal) by Various Metabolites.** *Proc. Soc. Exper. Biol. & Med.* 1959, Feb., v. 100, No. 2, 312–15, 1 fig.

Kethoxal (β-ethoxy-α-ketobutyraldehyde hydrate) has previously been shown to possess marked activity against certain viruses in the chick embryo [this *Bulletin*, 1957, v. 32, 1092] but has little or no therapeutic activity in animals. An explanation for this is offered here. Kethoxal has been found to combine with proteins and amino-acids at different rates and with different degrees of loss of activity: combination was particularly rapid and destructive of activity with cysteine and arginine. It is therefore thought to be "rapidly bound and inactivated in the complex animal system", whereas the retention of activity in the chick embryo is due to the "much simpler chemical environment and low protein content of the allantoic fluid". *L. P. Garrod*

HOLTERMANN, O. A., MERGENHAGEN, S. E. & MORGAN, H. R. **Factors related to Psittacosis Virus (Strain 6BC) Growth. V. Folic Acid-like Factor in Infected Cells.** *Proc. Soc. Exper. Biol. & Med.* 1959, Feb., v. 100, No. 2, 370–72, 1 fig. [13 refs.]

Folic acid is a vitamin requirement for L cells (mouse fibroblasts), but they support the growth of psittacosis virus when cultivated in a semi-synthetic medium. The authors showed that the 6BC strain of psittacosis virus growing in L cells was inhibited by sulphadiazine and that this inhibition was reversed by p-aminobenzoic acid (PABA). L cell cultures in monolayer were depleted of folic acid by growing them in a folic-acid-free semi-synthetic medium for 14 days. These cultures were then infected with the 6BC strain of psittacosis virus, control cultures receiving heated virus, and when cytopathogenic change began to appear in the former the flasks were frozen and thawed and their contents, after lyophilization, assayed for folic acid. The cultures of psittacosis virus contained more than twice the amount found in the uninfected controls. The authors consider that infection of the L cells, not capable themselves of making folic acid, has provided an enzyme or enzyme system able to do so, though whether this is part of the intact virus particle remains to be determined. *S. P. Bedson*

Strauss, J. & Šmejkal, F. Persistence viru ornitózy při hodnocení jeho citlivosti k penicilinu a chlortetracyklinu (aureomykoinu) u bílých myši. [**Persistence of Ornithosis Virus in Evaluation Experiments of its Sensitivity to Penicillin and Chlortetracycline (Aureomykoin) in White Mice**] *Českoslov. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 2, 73–83, 3 graphs. [Numerous refs.]

The English summary appended to the paper is as follows:—

“In the first experimental evaluation of the effect of penicillin and chlortetracycline—CTC (aureomykoin)—of Czechoslovak production on viruses the persistence of ornithosis virus in vivo was proved to be the result of a merely virostatic effect of CTC.

“The explanation seems to agree with the opinion that an effective antibiotic gives rise to certain forms of the developmental cycle of the ornithosis virus (initial bodies, plaques). These forms, however, in the absence of antibiotics, divide again into the elementary bodies, or they condition latency of the infection.

“The effectiveness of penicillin given in the highest doses (10 000—50 000 units per 1 ml) in vitro and in vivo in titration trials of ornithosis virus was not proved by the experiments performed, whereas CTC (1000—10 000 $\gamma$ per 1 ml/1000 $LD_{50}$ of virus) in vitro, and especially in vivo, acted partly in a virocidal, but, above all, in a virostatical way. Besides being effective after intraperitoneal administration, CTC had also a virostatic effect following peroral application when added to the Larsen diet.

“If virostatic doses of 1000—10 000 $\gamma$ CTC per 1 g of the Larsen diet were used the persistence of virus was proved in the spleen of mice which underwent inoculation with diluted virus and in which a clinical disease was not evoked as a result of the influence of antibiotics.

“The experimentally proved persistence of ornithosis virus following the prophylactic and therapeutic administration of CTC to white mice makes the fitness of a CTC application as a means of extermination of fowl ornithosis problematic. Only an experimental evaluation of CTC, or of another more efficient antibiotic in the practice of fowl-farming can solve the question of the importance of the possible virus persistence.”

Sarateanu, D. & Draganescu, N. **Experimental Infection of Cotton Rats with a Neorickettsial Agent isolated from a Case of Human Atypical Pneumonia.** *Acta Virologica.* Prague. 1959, Jan., v. 3, No. 1, 46–50, 6 figs. on 2 pls. [10 refs.]

The agent described in this paper was isolated from a woman with a pulmonary condition by the injection of exudate (presumably pleural) into eggs by the yolk sac route. It was lethal for mice by the nasal route and similarly so for the cotton rat. Acute and 14-day samples of the patient's serum showed a low increase in psittacosis group complement-fixing antibody and positive micro-agglutination of the “neo-rickettsial” antigen $Q_{18}$ of Giroud (titre not given). The agent was agglutinated by a rabbit-made $Q_{18}$ antiserum in a dilution of 1 in 1,000. [The neo-rickettsiae of Giroud *et al.* clearly belong to the psittacosis group but the precise relationship never seems to have been established.] *S. P. Bedson*

Sureau, P. & Brygoo, E. R., with the technical collaboration of Razafimahatratra. Culture du virus de la vaccine. II. Culture du virus de la vaccine sur cellules épithéliales de rein de veau en couche monocellulaire. [**Culture of Vaccinia Virus. II. Culture of the Virus on Monolayer Epithelial Calf Kidney Cells**] *Ann. Inst. Pasteur.* 1959, Mar., v. 96, No. 3, 343–51, 3 figs. [12 refs.]

Using monolayers of epithelial cells obtained by trypsinization of calf kidneys, the authors obtained “large amounts of highly virulent virus”. Starting with purified calf dermal lymph they passaged the virus in calf kidney cells. The titre increased from $10^{-4}$ at 1st passage to $10^{-10}$ at the 7th passage. [This is quite different from the findings reported by Cutchins & Warren (this *Bulletin*, 1958, v. 33, 708) who found a decrease in titre during adaptation of calf lymph vaccinia virus to bovine kidney cells.]

[For Part I, see *ibid.*, 1959, v. 34, 92.]

*Colin Kaplan*

Nagano, Y. & Kojima, Y. Inhibition de l'infection vaccinale par un facteur liquide dans le tissu infecté par le virus homologue. [**Inhibition of Vaccinial Infection by a Soluble Factor from Tissues Infected by Homologous Virus**] *C.R. Soc. Biol.* 1958, v. 152, No. 11, 1627–9, 2 figs.

This material was obtained from the dermal pulp of a rabbit infected with vaccinia virus. It was the final supernatant obtained after centrifugation of the crude extract at 3,000 r.p.m. for 15 minutes and then 3 successive centrifugations of that supernatant at 12,000 r.p.m. for 30 minutes. This procedure was thought to render the preparation non-infectious, but no evidence is offered in support of this belief.

When this supernatant was inoculated into rabbits by the intradermal route and a potent virus preparation was injected into the same sites 24 hours later, the virus titre reached $10^{-4\cdot5}$ or $10^{-5\cdot5}$. At control sites pre-inoculated with extract of normal rabbit skin, virus titres reached $10^{-7\cdot5}$ or $10^{-8\cdot5}$.

The greatest inhibitory effect was shown 24 hours after injection of the factor. A control of inactivated purified vaccinia virus also gave a very marked inhibitory effect 24 hours after injection. [This suggests that some sort of interference phenomenon may be operating.] The supernatant factor was stable at 56°C. for 30 minutes but not at 65°C. It was not inactivated by ultra-violet irradiation. It was not sedimented by centrifugation at 100,000 *g* for 2 hours and was not dialysable. *Colin Kaplan*

CASSEL, W. A. & FATER, Barbara. **Vaccinia Virus Hemagglutinin Inhibitor in Ascitic Fluids.** [Correspondence.] *Virology.* New York. 1959, Apr., v. 7, No. 4, 467–9.

BRANS, L. M. Variola-vaccine afkomstig van het kalf. Moderne bereidingswijze en gebruik. [**Preparation of Smallpox Vaccine on the Calf's Skin**] *Nederl. Tijdschr. v. Geneesk.* 1959, Mar. 7, v. 103, No. 10, 495–501, 7 figs. [11 refs.] English summary.

The author describes the method used in Holland for the production of smallpox vaccine from virus grown in the skins of calves. After a 7-day quarantine period and thorough clinical and bacteriological examination to exclude tuberculosis, foot and mouth disease, brucellosis and other diseases, the calf is vaccinated with sterile seed virus on an area of skin prepared as for surgery. The seed virus is second calf passage of a rabbit-adapted vaccinia strain. During the incubation period of 4 days elaborate precautions are taken to keep the vaccinated area uncontaminated. Before the vaccinial pulp is harvested the animal is anaesthetized, washed and then exsanguinated and killed. The preparation of the vaccine follows the method used in England and Denmark. Vaccine potency is determined by pock count on the chick embryo chorio-allantois. Bacteriological investigation is exhaustive. 70% of the vaccine batches reported were bacteriologically sterile; the remaining 30% contained less than 150 organisms per ml. *Colin Kaplan*

FISHER, Thelma N. & FISHER, E., Jr. **Effects of Cortisone and Herpes Simplex Virus on Metabolic Processes. I. Alterations in HeLa Cell Metabolism.** *Proc. Soc. Exper. Biol. & Med.* 1959, Apr., v. 100, No. 4, 780–86, 1 fig. [18 refs.]

KAPLAN, A. S. & VATTER, A. E. **A Comparison of Herpes Simplex and Pseudorabies Viruses.** *Virology.* New York. 1959, Apr., v. 7, No. 4, 394–407, 6 figs. [11 refs.]

"The properties of pseudorabies and herpes simplex viruses have been compared in tissue culture. These two viruses appear to be identical with respect to morphology and sensitivity to ether but are unrelated immunologically, and they differ in a number of other properties: pseudorabies virus is more thermostable, has a higher adsorption rate on rabbit kidney cells, and produces larger plaques which develop more rapidly than those of herpes simplex virus. The latent period of pseudorabies virus in monolayer cultures of rabbit kidney cells is 5 hours; in cell suspensions, 4 hours. In contrast, herpes simplex virus has latent periods of 8 hours and 5 hours, respectively. The two agents produce indistinguishable intranuclear inclusions, but herpes virus induces the formation of focal necrotic areas with characteristically rounded cells, whereas the predominant feature of infection with pseudorabies virus is the appearance of a syncytial layer with many nuclei."

STEWART, R. B. & MORGAN, H. R. **Studies on Cytotropism in Animal Viruses. I. Growth of Influenza Virus in Lung Cells derived from Hatched Chicks and Chick Embryos.** *J. Immunology.* 1959, Mar., v. 82, No. 3, 264–73, 7 figs. [20 refs.]

Cultures of lung or liver tissues from chick embryos at different stages of development (11 to 19 days' incubation) were shown to support the multiplication of influenza (PR8) virus. Lung tissues from newly hatched chicks were also able to support virus multiplication but to lower levels than those obtained with embryonic lungs. Virus multiplication occurred both at 37°C. and at 41°C. in embryonic lung cultures but only at 37°C. in lung cells derived from hatched chicks. The predominant cell type was epithelial in chick embryo lung cultures and fibroblastic in cultures of hatched chick lungs. It is suggested that this difference may explain the variations in virus multiplication observed in the 2 culture systems. *H. G. Pereira*

WHITE, D. O. & FAZEKAS DE ST GROTH, S. **Variation of Host Resistance to Influenza Viruses in the Allantois.** *J. Hygiene.* 1959, Mar., v. 57, No. 1, 123–33, 4 figs.

Factors affecting host susceptibility to influenza viruses were studied by infectivity titrations performed in fertile eggs and in surviving bits of chorio-allantoic membrane. Cell resistance to the infective action of different virus strains increased linearly with age of the embryos. This change in resistance was clearly demonstrated in titrations performed with surviving membrane bits and was not dependent on *p*H of the allantoic fluid of individual eggs. The lower infectivity end-points obtained by the use of old membranes was shown to be due to increased variation rather than to a uniform decrease of sensitivity to virus action.

Treatments leading to a lowering of membrane susceptibility to virus action and, at the same time, to an increase in egg to egg response variation included incubation of eggs at 35°C. rather than 38°C., maintenance of membranes *in vitro* before virus inoculation and use of inadequate maintenance media. *H. G. Pereira*

Woodhour, A. F. & Jensen, K. E. **Adsorption Characteristics of Influenza Viruses to Cholesterol and Fatty Acids.** *Proc. Soc. Exper. Biol. & Med.* 1959, Mar., v. 100, No. 3, 561–4, 1 fig.

Adsorption of influenza viruses to cholesterol was studied by measuring the haemagglutinin titres of effluents from chromatography columns or supernatants of virus-treated cholesterol suspensions. Addition of crude allantoic fluids to cholesterol columns resulted in complete adsorption of an Asian virus strain (A/Asian/Formosa/57), in partial adsorption of 2 other A strains (A/PR8/34 and A/PR301/54) and in no detectable adsorption of a B strain (B/GL/54). With virus preparations concentrated by high speed centrifugation and resuspended in phosphate-buffered saline, adsorption of strain B/GL could be detected and strain A/PR301 was adsorbed more effectively. By comparing virus adsorption in cholesterol columns and suspensions it was found that retention of strain B/GL in columns was due to mechanical trapping of virus aggregates. It was also shown that adsorption of A/PR301 to cholesterol is affected by inhibitory materials present in allantoic fluids. Such inhibitors have no action on adsorption of the Asian strain to cholesterol or on the adsorption of A and B strains to stearic acid. Animal inoculations of small doses of influenza viruses mixed with cholesterol or stearic acid gave rise to enhanced antibody responses. [See also Youngner & Noll, this *Bulletin*, 1959, v. 34, 687.]

*H. G. Pereira*

Arnoff, H. & Rafelson, M. E., Jr. **Studies on the Metabolism of Virus-Infected Tissues. II. The Effect of Influenza Virus on Ribonucleotide Metabolism in Chick Chorio-Allantoic Membranes.** *Arch. Biochemistry.* 1959, Apr., v. 81, No. 2, 421–9. [18 refs.]

Gan, K. H. & Warsa, R. **Antibacterial Activity of the Allantoic Fluid of Embryonated Eggs infected with Influenza Virus.** *Amer. J. Hyg.* 1959, Mar., v. 69, No. 2, 83–90.

Allantoic fluid, chorio-allantoic membrane and embryo homogenates from hen's or duck's eggs inoculated with PR8, FM1, Lee, Bonn, C or Djakarta strains of influenza virus were shown to contain a factor causing lysis of several bacterial species including *Bacillus subtilis*, *B. anthracis*, *B. cereus* var. *mycoides*, *Staphylococcus aureus*, *Staph. albus* and *Klebsiella rhinoscleromatis*. The lytic reaction occurred under optimal conditions at neutral *p*H and at temperatures between 40°C. and 45°C. The lytic factor is heat stable, being only slightly inactivated after heating at 120°C. for 30 minutes. It resists chloroform, alcohol and ether treatment and its activity is slightly reduced by 0·1% formalin or .5% phenol. It is not sedimented by centrifugation for 15 minutes at up to 7,500 r.p.m. (no G values given) and is partially retained by filtration through Seitz, Chamberland (L3), Berkefeld (N) filters or collodion membranes (no porosity given). Properties which distinguish the influenza lytic factor from lysozyme and from bacteriophage are presented. The lytic property of allantoic fluids from eggs infected with several influenza strains was not absorbed by chicken, guineapig or human erythrocytes and was not neutralized by homologous antisera. *H. G. Pereira*

Clark, R. J., Isaacs, A. & Walker, J. **Derivatives of 3:4-Xylidine and Related Compounds as Inhibitors of Influenza Virus: Relationships between Chemical Structure and Biological Activity.** *Brit. J. Pharmacol. & Chemotherapy.* 1958, Dec., v. 13, No. 4, 424–35. [29 refs.]

This paper describes the preparation of 83 compounds which were subsequently tested for capacity to inhibit the multiplication of influenza virus when added in a concentration of 0·1 mgm./ml. to tissue cultures of chick chorio-allantoic membrane. One of these, *N*-(2-piperidinoethyl)-3 : 4-xylidine dihydrochloride, which combined high virus-inhibitory activity with an apparent absence of tissue toxicity, was submitted to more detailed study, in the course of which it was found that this compound reduces the production of haemagglutinin to a greater extent than that of the soluble antigen of the virus. It had no effect on the multiplication of the virus in the allantoic cavity.

*L. P. Garrod*

Brug, J., De Bock, C. A., Moed, H. D. & Klein, A. J. **Antiviral Action of Derivatives of ω-Aminoacetophenone.** *Brit. J. Pharmacol. & Chemotherapy.* 1958, Dec., v. 13, No. 4, 404–10, 2 figs. [23 refs.]

A series of ω-aminoacetophenones was tested for activity against influenza virus by injection into the allantoic cavity 1 hour before inoculation with virus by the same route, and subsequent determinations of haemagglutinin titre. Some of these possessed high and others no activity, and some general principles relating structure to anti-viral activity as determined by this test are formulated, but their more general application is invalidated by the fact that tests by another method did not give corresponding results. This was admixture with virus *in vitro* and the determination at intervals thereafter of haemagglutinin titre and infectivity: some compounds inactive *in vivo* showed activity by this method. None of the compounds had any action in eggs inoculated *via* the yolk sac or on the infection in mice. *L. P. Garrod*

Kaji, M., Oseasohn, R., Jordan, W. S., Jr. & Dingle, J. H. **Isolation of Asian Virus from Extrapulmonary Tissues in Fatal Human Influenza.** *Proc. Soc. Exper. Biol. & Med.* 1959, Feb., v. 100, No. 2, 272–5.

Tissues obtained at post-mortem examination of 33 persons who had died of influenza were tested for the presence of virus by chick embryo amniotic inoculations. Asian influenza virus was isolated from lung or trachea of 25 of the 33 cases. Extrapulmonary tissues were shown to contain virus in 3 out of the 25 cases in which virus was isolated from the respiratory tract. Virus-positive tissues included spleen and lymph nodes in 1 case, liver, spleen, kidney and heart in another and tonsil in the third.

The possibility of contamination of extrapulmonary tissues during autopsy is discussed and considered to have been unlikely. *H. G. Pereira*

KALTER, S. S., CASEY, H. L., JENSEN, K. E., ROBINSON, R. Q. & GORRIE, R. H. **Evaluation of Laboratory Diagnostic Procedures with A/Asian Influenza.** *Proc. Soc. Exper. Biol. & Med.* 1959, Feb., v. 100, No. 2, 367–70, 1 fig.

Throat washings and serum specimens received for diagnosis of influenza during the Asian strain epidemic were tested by serological and virus isolation procedures. A comparison between complement-fixation and haemagglutination-inhibition tests was carried out with paired sera from 422 patients showing 4-fold or greater antibody rises and revealed positive results with both tests in 56% of cases, with complement-fixation only in 33% and with haemagglutination-inhibition only in the remaining 11%. The relationship between time of collection of serum and serological results was examined and the relative efficacy of the 2 tests is discussed in relation to the interval between onset of disease and time of bleeding. It is recommended that serum specimens should be tested routinely by complement-fixation and those giving a negative result should be tested by haemagglutination-inhibition.

A comparison between egg inoculation and tissue culture techniques for the isolation of Asian influenza virus from pathological specimens revealed a marked superiority of the former procedure. *H. G. Pereira*

JAWETZ, E., HANNA, L., SONNE, M. & THYGESON, P. **A Laboratory Infection with Adenovirus Type 8. Laboratory and Epidemiologic Observations.** *Amer. J. Hyg.* 1959, Jan., v. 69, No. 1, 13–20. [12 refs.]

A laboratory technician who had frequently handled type 8 adenovirus developed a typical attack of epidemic keratoconjunctivitis. The virus could be repeatedly isolated in tissue culture from conjunctival scrapings, but 2–5 passages with a total of 31–62 days of incubation were necessary before the presence of virus could be detected. Neutralizing antibody was present in the patient's serum on the 4th day of illness, but was not found in the sera of 5 members of the patient's family who were in close contact. In view of the low infectivity of the virus the authors suggest that it is transmitted by ophthalmological examinations and other manipulations of the eye, at least in North America, and is thus an iatrogenic disease.

*D. J. Bauer*

PEREIRA, H. G., ALLISON, A. C. & FARTHING, C. P. **Study of Adenovirus Antigens by Immunoelectrophoresis.** [Correspondence.] *Nature.* 1959, Mar. 28, v. 183, 895–6, 1 fig. [14 refs.]

Preliminary investigations with the gel diffusion technique have shown that partially purified preparations of type 5 adenovirus contain 3 antigens of smaller size than the virus particle, and in the present work the separation of these antigens by immuno-electrophoresis is described. The virus was grown in HeLa cell cultures and partially purified by fluorocarbon treatment [this *Bulletin*, 1959, v. 34, 503]. Electrophoresis was carried out in 2% agar in borate-phosphate buffer of *p*H 8·5 and ionic strength 0·05 at room temperature with a current of 20 ma for 7–8 hours. Antiserum was then placed in preformed side channels in the agar and allowed to react with the antigenic fractions for 5–6 days at 4°C. The gel was then washed, dried and stained with naphthalene black, which revealed the presence of 3 antigens with different electrophoretic mobilites, which were designated A, B and C. In a repetition of the procedure the located antigens were eluted separately into saline and examined further. A and B possessed complement-fixing activity, although in low titre, and B produced an early cytopathic effect in HeLa cells. Fraction B could not be demonstrated in material treated with trypsin.

*D. J. Bauer*

CULVER, J. O., LENNETTE, E. H., FLINTJER, J. D., STEVENS, Thirza E. & FOX, Virginia L. **Adenovirus Vaccine. A Study of the Complement-Fixing and Neutralizing Antibody Response.** *Amer. J. Hyg.* 1959, Mar., v. 69, No. 2, 112–19, 1 fig. [10 refs.]

The antigenicity of a vaccine containing formalin-inactivated adenovirus types 3, 4 and 7 was tested by a study of the complement-fixing and neutralizing antibody responses observed among 50 vaccinated volunteers and a comparable group of subjects given a placebo. Vaccination caused a significant rise in complement-fixation titres first detected after 4 or 5 days and remaining unchanged for the subsequent period of observation (70 days). Good rises in neutralizing antibodies for adenovirus types 3 and 7 were observed from 9 to 10 days after vaccination. Type 4 neutralizing antibody rises were minimal and equivocal.

[See also this *Bulletin*, 1957, v. 32, 405.]

*H. G. Pereira*

CULVER, J. O., LENNETTE, E. H. & FLINTJER, J. D. **Adenovirus Vaccine. A Field Evaluation of Protective Capacity against Respiratory Disease.** *Amer. J. Hyg.* 1959, Mar., v. 69, No. 2, 120–26. [12 refs.]

A vaccine containing formalin-inactivated adenovirus types 3, 4 and 7 was tested for efficacy in protecting military recruits against respiratory disease. A total of 4,355 recruits were included in the study and divided into vaccinated (30% of the total) and placebo groups. Influenza vaccines were being tested at the same time among the recruit population under study but the results of this part of the investigation are not presented in detail in the present paper and a small outbreak of type A influenza occurring during the period of observation affected the study groups only in a minor degree.

Effectiveness of the adenovirus vaccine was assessed in the first place by studying the incidence of respiratory disease in vaccine and placebo groups. A significant difference in disease incidence among the 2 groups was observed and the estimated effectiveness of the vaccine was 43%. Vaccine effectiveness based on rises of adenovirus complement-fixing antibody during the illness was also estimated and gave a value of 70% protection. Virus isolation studies showed that adenovirus infections occurring during the period of observation were caused mainly by adenovirus type 4. The relatively low level of protection conferred by vaccination is thought to be due at least in part to the poor antigenicity of the type 4 component of the vaccine used [see CULVER *et al.* above].

*H. G. Pereira*

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CULVER, J. O., LENNETTE, E. H., FOX, Virginia L. & FLINTJER, J. D. **A Long-Term Study of Antibody Response to an Adenovirus Vaccine and Observations on the Effect of Concurrent Adenovirus Disease.** *Amer. J. Hyg.* 1959, Jan., v. 69, No. 1, 38–48, 4 figs. [14 refs.]

The immune response to a vaccine containing types 3, 4 and 7 adenovirus has been followed over a period of 4½ months in a military company consisting largely of recruits. The company was divided into 4 groups; the first group received 2 doses each of 2 cc. of vaccine, the second group 2 cc. of vaccine and 2 cc. of a placebo, the third group 2 doses of placebo and the fourth group, which consisted of seasoned soldiers, received 2 doses of 1 cc. of vaccine, the interval between injections being 55 days in all groups. Before vaccination complement-fixing antibody titres of around 10 were found in the first 3 groups and 21 in the fourth group; the titre rose to around 34 in groups 1, 2 and 4 after vaccination and remained at this level over the period of observation; no booster response was therefore observed in group 4, which consisted of men who were presumed to have been exposed to infection already. A rise in titre to about the same level took place in group 3, and evidently represented a response to natural infection. No second rise in titre was observed in response to the second dose of vaccine. In titrations of neutralizing antibody an adequate rise in titre to types 3 and 7 was observed, but the response to type 4 virus was unsatisfactory.

*D. J. Bauer*

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CHANY, C., ROBBE-FOSSAT, F. & COUVREUR, J. Enquête sérologique sur le rôle épidémiologique d'un virus respiratoire nouvellement reconnu: souche EA 102 des myxovirus para-*influenzae* type 3. [**Serological Study of the Epidemiological Role of the New Respiratory Virus EA 102**] *Bull. Acad. Nat. Méd.* 1959, v. 143, Nos. 5/6, 106–10, 2 figs.

The recently described virus EA 102 [CHANY *et al.*, this *Bulletin*, 1959, v. 34, 503] was found capable of causing haemadsorption and was identified as myxovirus para-influenza type 3 [type 1 haemadsorption virus of CHANOCK *et al.*, *ibid.*, 1958, v. 33, 621]. Its importance in the aetiology of acute respiratory infections was investigated by means of serum-neutralization tests performed with acute and convalescent sera from 109 children admitted to hospital with acute respiratory syndromes and from 93 children hospitalized for other than respiratory diseases. Significant antibody rises were observed in 23·6% and 4·1% of respiratory and non-respiratory cases respectively. All but 1 of the patients with antibody rises were observed during the winter months of 1956–7 and 1957–8. The highest incidence occurred among children under 2 years of age. The disease associated with virus EA 102 was usually mild and of short duration but with frequent pulmonary involvement.

*H. G. Pereira*

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SCHULTZ, E. W. & HABEL, K. **SA Virus—a New Member of the Myxovirus Group.** *J. Immunology.* 1959, Mar., v. 82, No. 3, 274–8.

A virus (designated SA virus) was isolated from the brain of a hamster inoculated intracerebrally with fluid from first chick embryo allantoic passage of nasal washings from a patient with acute upper respiratory infection. The virus was propagated intracerebrally in hamsters causing spastic paralysis with an incubation period varying from 2 to 28 days. Hamsters can also be infected by the intraperitoneal, intraspinal, intradermal and intranasal routes. Suckling hamsters are more susceptible to intracerebral inoculation than adults. Other animals susceptible to intracerebral inoculation of the SA virus include 1-day-old and young adult chickens, Swiss mice, white rats and cotton rats. The virus can be propagated in fertile eggs inoculated by the allantoic route, in monkey kidney tissue cultures and possibly also in HeLa cell cultures. Virus multiplication in monkey kidney cells can be detected by the haemadsorption technique [this *Bulletin*, 1957, v. 32, 1203] and is followed by a cytopathic effect consisting mainly of syncytial formation. Virus-containing allantoic or tissue culture fluids are capable of agglutinating guineapig red cells. The haemagglutinin is associated with sedimentable virus and can be adsorbed to and eluted from red cells. Red cell receptors for SA haemagglutinin are destroyed by cholera vibrio receptor-destroying-enzyme. Neutralization of SA virus in monkey kidney tissue cultures gave positive results with human gamma-globulin, and normal monkey, guineapig and hamster sera but not with normal rabbit, horse, sheep, chicken and dog sera. The SA virus was not neutralized by antisera against GD VII and FA strains of Theiler's mouse encephalomyelitis, Columbia SK, Mengo, herpes simplex and pseudorabies viruses. It was also shown, by neutralization, haemagglutination-inhibition and complement-fixation tests, to be distinct from known members of the myxovirus group, including CA, Newcastle disease, mumps, Sendai, influenza A, B and C, and haemadsorption types 1 and 2 viruses. It is suggested that the SA virus is a new member of the myxovirus group and that it may be capable of causing human infections. Its role in the aetiology of human disease remains to be determined.

*H. G. Pereira*

PATOCKA, F., KUBELKA, V. & KORYCH, B. **A Comparison of the Biological Properties and Pathogenesis of Hog Encephalomyelitis and Human Poliomyelitis.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 1, 1–15, 4 figs. on 2 pls. [50 refs.]

MASCOLI, C. C., STANFIELD, L. V. & PHELPS, L. N. **Propagation of Poliovirus, Measles, and Vaccinia in Guinea-Pig Spleen Cell Strains.** *Science.* 1959, Apr. 3, v. 129, 894–5.

"A new mammalian cell strain was established from guinea pig spleen tissues and has shown interesting virus sensitivity. Several viruses have been successfully propagated in the cells. For one of these, poliovirus, it represents one of the two successful attempts at propagating the virus in nonprimate or nonhuman cultures."

CHANG, R. S., with the technical assistance of Helen LIEPINS. **Participation of Bicarbonate in RNA and Protein Syntheses as indicated by Virus Propagation in Human Cells.** *J. Exper. Med.* 1959, Mar. 1, v. 109, No. 3, 229–38. [18 refs.]

HeLa and human conjunctival cells slowly degenerate in bicarbonate-depleted medium (with special methods for $CO_2$ removal), but the effect is reversible by the addition of bicarbonate (GEYER and CHANG, *Arch. Biochem. & Biophysics*, 1958, v. 73, 500). Since bicarbonate is known to be a precursor of nucleic acids, the effect of bicarbonate depletion on the multiplication of Coxsackie B1, polio and vaccinia viruses was studied. It was found that bicarbonate depletion prevented the cytopathic effect and multiplication of Coxsackie B1 and vaccinia virus in these experiments (the observation period was limited to 5 days). The cytopathic effect of poliovirus was delayed but not prevented by bicarbonate depletion but the yield of virus was not greatly affected. The effects of bicarbonate depletion were reversible by bicarbonate, RNA, partially degraded RNA and pyrimidine nucleosides and nucleotides. DNA and its derivatives did not reverse the effect of bicarbonate even for the DNA-containing vaccinia virus. The effect of bicarbonate on the efficiency of plating of some strains (especially attenuated strains) of poliovirus has been reported previously [VOGT *et al.*, this *Bulletin*, 1958, v. 33, 891; HSIUNG and MELNICK, *loc cit.*]. *A. J. Beale*

FROTHINGHAM, T. E. **Effect of Aging and Rotation on Human Amnion Cell Response to Polio and Sindbis Viruses.** *Proc. Soc. Exper. Biol. & Med.* 1959, Mar., v. 100, No. 3, 505–10, 6 figs. [17 refs.]

Although it is known that cells in culture differ in their viral susceptibility from cells *in vivo*, and that the viral susceptibility of "transformed" cells is different from the cells from which they were derived [SHEFFIELD and CHURCHER, this *Bulletin*, 1957, v. 32, 816], the influence of age of primary cultures has been relatively little investigated. It was found that the young human amnion cultures (up to 14 days) infected with a Type 2 poliovirus adapted to the chick embryo [ROCA-GARCIA *et al.*, *ibid.*, 1953, v. 28, 481] showed much less marked cytopathogenic effect [CPE] than 30-day-old cultures when the tubes were not rotated. Rotation of the young cultures enhanced the CPE but it was still very much less than in older cultures. The effect was not due to a substance in the medium which might be removed by the extra fluid changes given to older cultures. The multiplication of poliovirus was also delayed in young cultures, although the final titre was similar to that found in older cultures. A variety of other polioviruses, both virulent and attenuated, but not adapted to the chick embryo were not influenced by the age of the amnion cultures.

Sindbis virus [TAYLOR *et al.*, *ibid.*, 1956, v. 31, 874] also showed more marked CPE in older than in younger cultures. The yield of virus was also higher in 30-day cultures. The results in young cultures were somewhat variable, sometimes marked CPE was noted, at other times little or none. Rotation of the young cultures did not enhance the cytopathic effect. *A. J. Beale*

LIKAR, M. & WILSON, D. C. **Observations on the Interaction of Poliovirus and Host Cells *in vitro*: II. The Action of Insulin.** *Brit. J. Exper. Path.* 1959, Apr., v. 40, No. 2, 149–54, 3 figs.

Previously the authors have reported [this *Bulletin*, 1959, v. 34, 398] that incubation of tissue cultures at 39·5°C. increased the yield of poliovirus (Mahoney strain of Type 1) nearly 10-fold compared with cultures grown at 37°C. They now report that insulin produces a similar enhancement of the yield of Type 1 poliovirus (Mahoney and Brunhilde strains) in monkey kidney, HeLa and human amnion cells. The dose of insulin achieving maximum effect (about a 10-fold increase in titre) was 5 to 0·01 of an international unit per ml. in the cultures for 66 hours or more before virus infection. The insulin-containing medium was renewed daily. The effect of insulin was abolished at 39·5°C. or above. At 39·5°C. both insulin-treated and control cultures gave the same yield which was about 10-fold above the titre at 37°C. without insulin. On the basis of these results the authors suggest that poliovaccine manufacturers could boost virus titres [and therefore presumably antigenicity] by the use of insulin or 39·5°C. for growing cells for virus infection. They also obtained higher titres with trypsinized cell sheets than with Maitland type cultures of monkey kidney cells.

[The strains of poliovirus for which these effects have been demonstrated are not those incorporated in British poliovaccine.] *A. J. Beale*

MCBRIDE, W. D. **Antigenic Analysis of Polioviruses by Kinetic Studies of Serum Neutralization.** *Virology.* New York. 1959, Jan., v. 7, No. 1, 45–58. [19 refs.]

DULBECCO *et al.* [this *Bulletin*, 1956, v. 31, 959] devised a method of studying the kinetics of animal virus serum neutralization similar to that used by bacteriophage workers. This method has been used to study the antigenic characters of several Type 1 poliovirus strains and 2 strains each of Type 2 and 3. The velocity constants (K) for the rate of inactivation of the various strains in homologous and heterologous sera were determined. In order to facilitate comparisons of K values these were "normalized" by correcting the value in terms of the value obtained with homologous serum which was considered as 100. It was found that the K values uniquely identified the virus strains. It was found that strains isolated from 1 area in 1 year were more closely related than strains isolated earlier. There did not appear to be any recurrence of the strains with the antigenic character of Mahoney in the years since its first isolation. Sera obtained late in the course of immunization of animals showed broader specificity. It was found that the K values were the same for virus grown in monkey kidney, HeLa cells with horse serum and in skin cells with rabbit sera with antisera prepared against virus grown in monkey kidney cells. It was also found that the antigenic type was a very stable character, several substrains of Mahoney being indistinguishable and efforts to isolate antigenic mutants were unsuccessful. The value of this technique for classification of strains, for epidemiological and genetic studies is mentioned.

[This valuable paper should be consulted for the full technical details.] *A. J. Beale*

ROIZMAN, B., MAYER, M. M. & ROANE, P. R., Jr. **Immunochemical Studies of Poliovirus. IV. Alteration of the Immunologic Specificity of Purified Poliomyelitis Virus by Heat and Ultraviolet Light.** *J. Immunology.* 1959, Jan., v. 82, No. 1, 19–25, 2 figs. [12 refs.]

LE BOUVIER [this *Bulletin*, 1956, v. 31, 467] showed that heat and ultraviolet light treatment of crude tissue culture fluids infected with poliomyelitis virus causes a change in reactivity of the antigen in complement-fixation tests. The treated antigens react more frequently with acute sera from patients suffering from poliomyelitis and more rarely with convalescent sera and also tend to give heterotypic cross reaction. On the other hand, fresh unheated antigens yield the highest frequency of positive reactions with convalescent phase sera and are in general type specific. In a previous communication the authors [*ibid.*, 1958, v. 33, 1094] have described 4 kinds of virus particles in infected monkey kidney tissue culture fluids. These are designated ID +, NID +, NID − and NIC −, the unheated antigens react as D and the treated ones as C. [I and NI refer to presence or absence of infectivity, D and C denote the serological specificity of the particle.] The effect of heat at 56°C. and ultraviolet light upon ID + and NID + particles has been investigated. It was found that heat at 56°C. destroyed the infectivity at about the same rate that the immunological specificity was changed from D to C, the evidence being strong that the NIC particles were in fact degraded D particles. On the other hand, ultraviolet light was found to destroy the infectivity much more quickly than it affected the D antigen. Although heated D particles are thought to be degraded to C it is found that the behaviour on ultracentrifugation of heated D (NID or ID) is different from that of NIC present in the infected tissue culture fluid. It is thought that this difference is due to aggregation of the denatured D particles. *A. J. Beale*

SPRUNT, Katherine, REDMAN, Winifred M. & ALEXANDER, Hattie E. **Combination of Antigenic Traits of Type 1 and Type 2 Poliovirus.** *J. Immunology.* 1959, Mar., v. 82, No. 3, 232–40, 6 figs.

In an earlier paper [SPRUNT *et al.*, this *Bulletin*, 1955, v. 30, 1119] the authors described experiments suggesting that after the growth of polioviruses 1 and 2 in a 1 : 1 ratio in the same monkey kidney cell new particles appeared which were genetically stable and combined the Type 1 and 2 antigenic character. This work was carried out by relatively crude methods of analysis: terminal dilution for clone isolation and tube neutralization tests. In the present paper the progeny virus previously described has been subjected to more refined analysis by the plaque technique for both cloning and antigenic analysis. The number of plaques were counted in the presence of normal serum and Type 1 and 2 antiserum and the presence of doubly neutralizable particles was expressed as a titre discrepancy, *i.e.*, the per cent of total particles revealed by summing the counts of the 2 assays in the presence of antiserum. The presence of doubly neutralizable particles was confirmed and they were still present in an undiminished degree after 7 plaque-to-plaque passages.

[These results differ from those of ITOH and MELNICK [*ibid.*, 1959, v. 34, 836] in that the particles were stable on passage (*i.e.* not explicable as phenotypic mixing) and that the discrepancies were for the most part less, *i.e.* only singly neutralizable and doubly neutralizable particles were present. This could be explained by recombinants predominantly of one antigenic type but with minor antigenic components of the other type. SPRUNT *et al.* state that the elucidation of the mechanism of the formation of doubly neutralizable particles must await more work.]

*A. J. Beale*

CRAIG, D. E. & BROWN, G. C. **The Relationship between Poliomyelitis Antibody and Virus Excretion from the Pharynx and Anus of Orally Infected Monkeys.** *Amer. J. Hyg.* 1959, Jan., v. 69, No. 1, 1–12. [11 refs.]

The influence of antibodies acquired either from infection or killed vaccine on the fate of monkeys subsequently orally infected with poliovirus (mainly Mahoney Type 1 strain) was studied. In the dosage employed control animals developed paralysis (13 out of 14) and excreted virus in their faeces for the first 3 days as a rule then, after a break of 1 or 2 days, started excretion again till death or the appearance of antibodies. Virus is present in the pharynx from the day of infection and no break in excretion occurs.

Only 1 out of 10 animals with antibodies induced by live virus became paralysed and only 1 excreted virus in the throat although all excreted virus for a short period in the faeces. The antibody levels in these monkeys were usually higher than those in vaccinated animals but only 1 of the animals showed a rise in titre 21 days after infection. 6 out of 16 monkeys with antibodies from poliovaccine became paralysed. These animals had in general lower antibody titres than the group given living virus and 5 of them excreted virus in the pharynx. All of them excreted virus in the stools. The pattern of virus excretion in the vaccinated animals without antibodies closely approximated that of controls although some protection was conferred (9 out of 14 paralysed). The vaccinated animals with antibody showed a booster response to infection, not only achieving high titres but also developing antibodies more quickly than control animals (in 7 or less days opposed to 10–14 days). The presence of heterologous antibodies did not influence the excretion of virus. Immune monkeys appeared to cast off virus quickly from the alimentary canal, developing a booster response if the antibody level was low.

It is pointed out that these results are in agreement with those of HOWE [this *Bulletin*, 1958, v. 33, 824] in chimpanzees but at variance with those of HORSTMANN and her colleagues in children [*ibid*., 1958, v. 33, 321, 998]. They found a more marked difference between the pharyngeal and faecal excretion of virus in children with naturally or vaccine acquired antibodies.

*A. J. Beale*

GOLDBLUM, N., MERCADO, A., FOGEL, Aliza & CYMBALISTA, S. **Effect of Filtration Procedures on Immunogenic Activity and Safety of Formalinized Poliomyelitis Vaccine (Salk Type).** *Proc. Soc. Exper. Biol. & Med.* 1959, Feb., v. 100, No. 2, 276–9.

The senior author with other colleagues has previously described a technique for making poliovaccine [GOLDBLUM *et al*., this *Bulletin*, 1958, v. 33, 622]. Following U.S. recommendations they performed 2 filtrations, one before and one during the formaldehyde inactivation process; both filtrations were through Seitz sterilizing pads since sintered glass filtration was found to give inconsistent inactivation. It was found that pretreatment of the pads with medium 199 instead of Hanks salt solution reduced the loss of infectious virus to negligible amounts during filtration. However, even so the potency of monovalent pools was much greater if the second filtration was omitted or performed through a glass filter. Extinction limit potency titres in guineapigs were always over $10^{-2}$ and often $10^{-3}$ if the second filtration was omitted whereas if it was included, titres rarely reached $10^{-2}$. The omission of the second filtration was not at the expense of safety, although exact details of safety testing are not given. However, the vaccines were used in the field without untoward results.

[The statement that the Seitz pads treated with 199 do not successfully adsorb infectious poliovirus is not adequately documented. Titres on the bulk filtrate may not reveal large losses in the first runnings. More adequate methods of treatment of Seitz filter pads are known, see for example KANAREK *et al*., *VIIth International Congress for Microbiology—Abstracts of Communications*, Stockholm, Aug. 4–9, 1958, p. 367.]

*A. J. Beale*

SABIN, A. B. **Present Position of Immunization against Poliomyelitis with Live Virus Vaccines.** *Brit. Med. J.* 1959, Mar. 14, 663–80, 5 figs. [33 refs.]

In this long paper Dr. Sabin summarizes his views on the present status of attenuated poliovaccine. The paper is a summary and should be read by all interested in the prevention of poliomyelitis. There are detailed descriptions of his techniques of intracerebral and intraspinal inoculation. The usual technique of intracerebral inoculation involving 0·5 ml. into each thalamus is considered too traumatic for measuring strictly intracerebral virulence, because virus may spread to the spinal cord. A dose of 0·5 or 1 ml. into 1 site is preferred. For intraspinal inoculation 0·1 ml. is used. Criticism of the techniques of other workers is made on 2 grounds, either they are too insensitive because they use the wrong site or, because multiple or too large doses are given, too sensitive. A fallacy is involved in assessing increased virulence of poliovirus excreted by vaccinated individuals by inoculating the strains directly into the CNS, since pathogenic strains must probably also have the capacity to multiply first in extraneural tissue from which they spread to the CNS. There is evidence that many of the strains isolated from vaccinated individuals contain many non-cytopathogenic particles which may not be able to multiply in extraneural tissues. Also the conditions of culture of the strains before testing are most important to prevent the selection of more virulent variants by low *p*H for example.

The increase in virulence of strains excreted by vaccinated individuals is illustrated by studies on 5 “ triple-negative ” children. No satisfactory *in vitro* markers are yet known for neuropathogenicity, resort has to be made to the animal test. Virus has been found to spread from vaccinated to non-vaccinated people in trials in Russia and elsewhere but no evidence of progressive increase in virulence has been observed. The importance of alimentary immunity, not reflected in antibody titre, conferred by natural or attenuated poliovirus but not by killed vaccine is stressed. The details of manufacture and testing of the large lots of attenuated vaccine are described. [Incidentally, the testing methods detected an unidentified virus as a contaminant in the vaccine used by COURTOIS *et al*., this *Bulletin*, 1958, v. 33, 1022.] Finally, some account of the many trials of attenuated vaccine under way is given.

*A. J. Beale*

BARRON, A. L. & KARZON, D. T. **Cultivation of Enteroviruses in Hamster Kidney Tissue Culture.** *Proc. Soc. Exper. Biol. & Med.* 1959, Feb., v. 100, No. 2, 316–20, 3 figs. [14 refs.]

Primary hamster kidney cultures were tested for susceptibility to enterovirus and a few other viruses.

The following viruses produced cytopathic effects, for enteroviruses the prototype strains were employed: Coxsackie A9 and B1–5 (although B5 was slow), ECHO 9 and 10, herpes simplex, influenza A (Asian strain not PR 8), vaccinia and Newcastle disease virus. The following viruses did not produce any cytopathic effect: poliovirus 1, 2, 3, ECHO 1–19 (except 9 and 10) and canine distemper virus. Only some strains (2 out of 27) of ECHO 9 would produce effects in hamster kidney. Monkey kidney cultures were more sensitive for primary isolation of Coxsackie B viruses, although after adaptation to hamster kidney the enteroviruses tested gave as high titres in either type of kidney culture. *A. J. Beale*

TAKEMOTO, K. K. & HABEL, K. **Virus-Cell Relationship in a Carrier Culture of HeLa Cells and Coxsackie A9 Virus.** *Virology*. New York. 1959, Jan., v. 7, No. 1, 28–44, 4 figs. [20 refs.]

Coxsackie A9 virus infection of HeLa cells has been found to result in a virus carrier culture, if the virus dose inoculated is too small to produce a visible cytopathic effect or by allowing the few cells that survive a larger dose to grow out and repopulate the culture vessel. Since it was found that the cultures could be cured by antiserum, that only a few of the cells were infected and that the cells were not completely resistant to reinfection, it was concluded that the cells were not latently infected (*i.e.* that it was not analogous to a lysogenic bacterial culture). Removal or lowering of the serum concentration caused the cells to degenerate. Carrier cultures were obtained with HeLa cells grown in human, horse or calf serum. The presence of antibodies in the serum was not essential, although the human sera contained low levels of antibody detectable by the method measuring viral destruction by antiserum. The cells isolated from a carrier culture by cloning single cells or curing the culture with antiserum were more resistant to Coxsackie A9 than normal HeLa cells. Also the virus isolated from carrier cultures was altered. The virus was no longer pathogenic for suckling mice. It produced smaller plaques on monkey kidney cells, and in HeLa cells showed the same titre by observation of the cytopathic effect as by subculture in monkey kidney cells, unlike the parent strain. It also showed slight antigenic differences from the monkey kidney propagated virus. Coxsackie A9 (both the carrier strain and the monkey kidney strain) is very unstable at 37°C.

*A. J. Beale*

ITOH, H. & MELNICK, J. L. **Double Infections of Single Cells with ECHO 7 and Coxsackie A9 Viruses.** *J. Exper. Med.* 1959, Apr. 1, v. 109, No. 4, 393–406, 1 fig. [14 refs.]

The progeny resulting from mixed infection with Coxsackie A9 and ECHO 7 virus grown in rhesus and patas monkey kidney cells were studied by harvesting the yield from individual cells isolated in microdrops of nutrient under oil. The progeny were tested for growth on cells with normal monkey serum, or the antiserum to one of the parental types in the overlay. The presence of doubly neutralizable particles was inferred if the number of the plaques in either of the 2 antiserum assays was only 25% or less of the control assay under normal serum. 36% of the cells in microdrops yielded virus, whereas virus was only very rarely present in microdrops without visible cells. 15 of 102 microdrops containing single cells yielded doubly neutralizing particles, 53 yielded virus of one or other antigenic type, but in 34 drops there was some evidence of doubly neutralizable particles, *i.e.* the sum of the counts in antiserum were less than in controls.

After passage of plaque-isolated virus only 1 or other of the parental types was revealed by neutralization tests, and similarly only those tubes yielding Coxsackie A9 were pathogenic for suckling mice. It was therefore concluded that the doubly neutralized particles were examples of phenotypic mixing. Since the particles did not breed true there was no evidence for genetic recombination. *A. J. Beale*

CLOUGH, P. W. **Coxsackie Viruses as a Cause of Disease in Man.** [Editorial.] *Ann. Intern. Med.* 1959, Apr., v. 50, No. 4, 1062–8. [22 refs.]

RAPMUND, G., GAULD, J. R., ROGERS, N. G. & HOLMES, G. E. **Neonatal Myocarditis and Meningoencephalitis due to Coxsackie Virus Group B, Type 4. Virologic Study of a Fatal Case with Simultaneous Aseptic Meningitis in the Mother.** *New England J. of Med.* 1959, Apr. 16, v. 260, No. 16, 819–21.

“Isolation and serologic studies are described in a fatal case of neonatal myocarditis and meningoencephalitis due to Coxsackie virus Group B, Type 4, with simultaneous aseptic meningitis in the mother due to the same organism. A satisfactory antibody response to infection was demonstrated in the new-born infant both by tissue-culture metabolic-inhibition and by in vivo suckling-mouse protection tests.”

CAMAIN, R. & BRES, P. Contribution à l'étude du virus de Coxsackie. Evolution des lésions chez le souriceau. [**Contribution to the Study of Coxsackie Virus. Evolution of the Lesions in Suckling Mice**] *Ann. Inst. Pasteur.* 1959, Mar., v. 96, No. 3, 376–9.

The time sequence of the appearance of symptoms and histological lesions in 48-hour-old mice inoculated with Coxsackie A type 6 either intracerebrally or intraperitoneally is described. Lesions regularly appeared first in the pelvic muscles giving lower limb paralysis and later spread to vertebral, intercostal, scapular and pulmonary muscle groups. These lesions were first oedematous, then inflammatory. *A. J. Beale*

McLAREN, Anne & SANDERS, F. K. **The Influence of the Age of the Host on Local Virus Multiplication and on the Resistance to Virus Infections.** *J. Hygiene.* 1959, Mar., v. 57, No. 1, 106–22, 4 figs. [24 refs.]

The susceptibility of young mice to infection with several neurotropic viruses decreases with age. Thus the infectivity of EMC virus for mice decreased markedly with age when given by mouth, intramuscularly or intraperitoneally but not by the intracerebral route. With Coxsackie viruses (A-4 Texas and B-1 Conn 5 strains were used) a similar effect was noted with either the intracerebral or peripheral routes. It was found that there was an exact correlation between susceptibility of the mice and the ability of virus to multiply locally after small doses into muscle or brain.

4 hypotheses were examined as an explanation of these observations.

1. Above a certain age muscles may become unable to support virus multiplication. This explanation fails since there is progressive increase in resistance with age and large doses may still multiply in muscles.
2. The rate of multiplication might be delayed with age. This would cause longer incubation periods with age but would not prevent death. This was not observed.
3. Hypothesis 2 may hold since the incubation period is prolonged and then the immune mechanism may lead to recovery. If this explanation was true the incubation period should increase more with falling virus dose in older than in younger animals, but this was not observed.
4. The data were best explained by assuming that the permeability of the cells for virus declined with age. This hypothesis received some additional support from the finding that 12% physostigmine sulphate (which increases cell permeability Greig and Mayberry, *J. Pharmacol. & Exper. Therap.*, 1951, v. 102, 1) injected into the same muscle as the GD VII strain of encephalomyelitis virus (a virus showing similar age susceptibility effect) increased the susceptibility of relatively resistant mice nearly 10-fold. *A. J. Beale*

Lehmann-Grube, F. & Syverton, J. T. **Thermal Stability of ECHO Viruses in Cell Culture Medium.** *Amer. J. Hyg.* 1959, Mar., v. 69, No. 2, 161–5, 1 fig. [14 refs.]

The rate of inactivation of ECHO virus prototypes 1–20 and poliovirus Type 1 (Mahoney strain) at 37°C. in a medium of Hanks salt solution, 0·5% lactalbumin hydrolysate and 2·5% calf serum at a *p*H of 7·4–7·8 was investigated. ECHO 10 was studied in medium without serum. Titrations for residual virus were performed in monkey kidney cultures. The rates of inactivation varied markedly with different strains. The half life of virus at 37°C. was estimated for 6 of the strains on the assumption of a linear rate of inactivation. The half lives were: poliovirus Type 1, 47 hours; ECHO 1, 24 hours; E4, 18 hours; E6, 40 hours; E9, 19 hours; and E20, 2·5 hours. *A. J. Beale*

Hammon, W. McD., Yohn, D. S., Pavia, Rose A. & Sather, Gladys. **Echo Virus Type 13. I. Isolation and Characteristics.** *Proc. Soc. Exper. Biol. & Med.* 1959, Feb., v. 100, No. 2, 425–9. [13 refs.]

The original prototype strain of ECHO 13 (Hamphill 2-188-20) has been found to be contaminated with ECHO 1 virus. ECHO 13 was obtained from the mixture by the use of ECHO 1 antiserum. Also ECHO 13 was re-isolated from the original stool swab and plaque purified. Similarly, another ECHO 13 isolate was plaque purified. This latter strain (Del Carmen 11-4-1) has been adopted as the new prototype ECHO 13 strain. It is slightly broader antigenically than the previous prototype and grows better in tissue culture. The strain shows no cross reactions with other ECHO serotypes (the cross reactions with type 1 and 8 are eliminated in the pure prototype). The strain is not pathogenic for suckling mice, but 2 monkeys showed chronic meningoencephalitis 21 days after an intracerebral and intraspinal dose of virus. The virus grows well with cytopathic effects in monkey kidney cultures and in the H.Ep. 2, Detroit 504 Fb-L cell lines. Results in HeLa cells are variable, and growth does not occur in the monkey heart line cells or primary cultures of hamster or gerbil monkey kidney. The plaque morphology is that of Hsiung and Melnick's [this *Bulletin*, 1957, v. 32, 1205] group A (types 1–6, 9, 11, 13 and 14). It shares with types 3, 6 and 11 the capacity to agglutinate human group O red cells at 4° or 25°C. but not 37°C. *A. J. Beale*

Casals, J. **Viruses: The Versatile Parasites. I. The Arthropod-Borne Group of Animal Viruses.** *Trans. New York Acad. Sci.* 1957, Jan., Ser. 2, v. 19, No. 3, 219–35, 2 figs. [13 refs.]

This is a valuable account of the arborviruses; the table shows the grouping clearly.

“Arthropod-borne (Arbor) animal viruses can be assembled in sharply defined groups on the basis of serological interreactions detected specifically by hemagglutination inhibition tests. At present, the three such groups that have been characterized have been designated A, B, and C; the indications suggest that additional serological groupings exist. Although several Arbor viruses have not been placed in any of the described serological groups and may remain as isolated entities, the indications are that group similarities are fairly common among many of the Arbor viruses and that the underlying mechanism is probably the result of common antigenic constituents among the members.

“As the work with these agents progressed, it became more challenging to determine whether the grouping property of Arbor viruses represented more than a simple academic taxonomy. From the outset there was no doubt that this grouping constituted a helpful device for facilitating identification of new isolates. As the evidence accumulated, however, the different groupings revealed profound relationships to the course of events in natural infections of man and lower animals. Thus, mutual interactions between two viruses of a group can be detected in experimental animals; these result in serological responses beyond the ability of each one separately. The evidence gathered seems to indicate that this is also the case in man naturally infected. In experimental animals, the capacity of an agent to protect against another virus of the same group could be demonstrated. The question whether a human population that has been exposed to infection by a virus

TABLE 1

CLASSIFICATION OF ARTHROPOD-BORNE ANIMAL VIRUSES

| *Group A* | *Group B* | | *Group C* | *Ungrouped* | |
|---|---|---|---|---|---|
| Chikungunya | California bat | SA H 177 | Be An 15 | Anopheles A | Eg Ar 1152 |
| Eastern EE* | Dengue, type 1 | SA H 336 | Be An 17 | Be An 73 | Len 731-19 |
| Mayaro | Dengue, type 2 | St. Louis | Be An 848 | Be An 277** | Rift Valley fever† |
| Semliki Forest | Ilhéus | Uganda S | | Be H 151** | Sandfly fever, Naples† |
| Sindbis | Japanese B | West Nile | | Bunyamwera† | Sandfly fever, Sicilian† |
| Venezuelan EE* | Louping ill | Yellow fever | | Bwamba‡ | SAT Ar 53§ |
| Western EE* | Murray Valley E. | Zika | | California, Hammon-Reeves | Tr 3587 |
| | Ntaya | | | Colorado Tick fever | Tr 8900 |
| | Russian SS | | | Eg Ar 492 | Tr 9760§ |
| | SAT Ar. 94 | | | Eg Ar 1095 | Wyeomyia |

All viruses in Groups A, B, and C produce hemagglutinins; louping ill not tested.

*EE = equine encephalomyelitis.

**Be An 277 and Be H 151, although not identical, are related by CF.

†These viruses produce hemagglutinins.

‡There seem to be several agents, isolated in South Africa, that are very closely related to Bwamba, but are not identical with it.

§SAT Ar 53 and Tr 9760, distantly related by CF.

will show an increased resistance against invasion by another microorganism of the same group must be left unanswered. In this connection, however, one must note the protection secured by appropriate tests against yellow fever virus with sera from persons who had presumably been infected previously with dengue. The corollary problem, whether one virus of a group is capable of preventing or modifying infection, not only against itself, but also against all or many other members of that group, (as, for instance, in vaccination), awaits further experimentation. The aforementioned results and observations provide a logical basis for such a notion."

DICK, G. W. A. Les maladies à virus sous les tropiques. [**Virus Disease in the Tropics**] *Bull. Soc. Path. Exot.* 1958, Sept.–Oct., v. 51, No. 5, 709-17.

Some of the main virus infections peculiar to the tropics—mainly arborviruses—are briefly reviewed. The possible epidemiological importance of the antigenic relationships within certain groups of these viruses—notably group B of arborviruses—is discussed. Urban yellow fever in South America is cited as an example where vector control has virtually eradicated human infections—but such success is impossible with most other arborvirus infections. Their control depends on reaching a full understanding of their ecology and particularly their animal reservoirs.

*C. E. Gordon Smith*

JUBA, A. & PINTÉR, M. Histopathologie der mit einheimischem Virus ausgelösten experimentellen Zeckenenzephalitis. [**Histopathology of Experimental Tick-Encephalitis elicited by Virus isolated in Hungary**] *Acta Morphologica.* Budapest. 1959, v. 8, No. 4, 415–24, 8 figs. [19 refs.]

The English summary appended to the paper is as follows:—

"The histopathology of tick encephalitis induced in mice by the subcutaneous and intracerebral inoculation of large doses of the virus strain $KEm_1$, one isolated in Hungary, has been studied. Animals surviving inoculation by 1 to 6 days were subjected to histological analysis. Both modes of administration produced inflammatory changes as early as the first day, often in the frontal-basal area. Affections of the cells of Purkinje and of the ganglionic cells in the anterior horn were prominent among parenchymatous changes; in response to intracerebral inoculation, these developed during the first day already, whereas they were observable only after a few days following subcutaneous inoculation. In the brain of the intracerebrally inoculated animals, along the injection wound severe lesions of ganglionic cells, invasion by leucocytes and later intense microglial proliferation were detectable. There was no evidence to indicate that the virus could be propagated in the central nervous system along the long pathways or along the CSF spaces, or that it would reach the central nervous system along the peripheral nerves. Haematogenous dissemination appears to play an important role in the spread of virus in the nervous system."

MACNAMARA, F. N., HORN., D. W. & PORTERFIELD, J. S. **Yellow Fever and Other Arthropod-Borne Viruses. A Consideration of Two Serological Surveys made in South Western Nigeria.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1959, Mar., v. 53, No. 2, 202–12. [15 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 819.]

MATUMOTO, M., SABURI, Y. & NISHI, I. **Rift Valley Fever Virus in the One-Day-Old Chick Embryo.** *J. Immunology.* 1959, Mar., v. 82, No. 3, 219–25, 3 figs. [22 refs.]

The inoculation of the embryos was with 0·1 ml. into the yolk sac. Both pantropic and neurotropic viruses reached a maximum titre of about $10^{-6}$ after 2–3 days' incubation. In titrations 0·4 to 1·8 log higher titres were obtained in mice than in embryos. Eggs incubated 1–7 days were inoculated: in those incubated 1–3 days the titres of virus obtained were of the same order but in older eggs there was progressively less multiplication until none could be detected in 7-day eggs. The viruses were successfully passed serially in 1-day embryos with titres fluctuating between $10^{-4\cdot5}$ and $10^{-7\cdot7}$. Passage did not, however, affect the pathogenicity of the viruses for older eggs or for mice.

*C. E. Gordon Smith*

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## IMMUNITY

TURK, J. L. **Immunological Activity of Precolostral Calf Serum.** [Correspondence.] *Nature.* Mar. 21, v. 183, 838.

New-born calf sera collected before suckling, that is before any maternal immunity in the colostrum could be transferred or before the development of normal antibodies was possible, were titrated for bactericidal activity; estimates were also made of the properdin and complement titres. The bactericidal activity was tested against a wide range of smooth bacterial cultures and found to be negligible. On the other hand the sera were highly bactericidal against rough strains of the typhoid bacillus and Shiga's dysentery bacillus; this effect was completely removed when the sera were absorbed with zymosan. The properdin levels were within ± 50% of those found in normal adult bovine serum and the conglutinating complement titres were between 16 and 32. The author considers that the observed bactericidal effect is probably due to the interaction of properdin and complement and that properdin and the components of complement necessary for this effect are developed by the foetus *in utero* and are not related to the production of normal antibodies that appear in the calf as a function of age.

*H. J. Bensted*

ARNON, H., SALZBERGER, M. & OLITZKI, A. L. **The Appearance of Antibacterial and Antitoxic Antibodies in Maternal Sera, Umbilical-Cord Blood and Milk: Observations on the Specificity of Antibacterial Antibodies in Human Sera.** *Pediatrics.* Springfield, Ill. 1959, Jan., v. 23, No. 1, Pt. 1, 86–91. [25 refs.]

This paper describes an investigation into the placental transfer of *Escherichia coli* antibodies compared with that of diphtheria antitoxin. Maternal sera, umbilical cord blood and human milk were examined by haemagglutination tests, diphtheria antitoxin titrations, bactericidal tests and electrophoresis. It was found that *E. coli* and *Shigella sonnei* antibodies pass freely to the mother's milk but have limited transfer across the placenta, while diphtheria antitoxin passes to both in almost unlimited amounts. Electrophoresis tests on maternal and cord blood did not show that these transfer differences could be correlated with differences in placental transfer of various serum fractions. Absorption experiments showed that normal adult sera contain specific and non-specific somatic antibodies of *E. coli* 055 and 0111, *Sh. sonnei* and *Salmonella paratyphi B.*

*John S. Stevenson*

EDWARDS, M. S., GRIFFITHS, L. L. & SWIFT, P. N. **Cellular Immunity at Birth. The Mechanism and Nature of the Phagocytic Response.** *Arch. Dis. in Childhood.* 1958, Dec., v. 33, No. 172, 512–19, 3 figs. [12 refs.]

The phagocytic activities of maternal and infant leucocytes obtained from cord blood have been compared. The activity of the leucocytes was measured by determining the percentage which ingested one or more cells of a killed yeast cell suspension. The leucocytes, both maternal and infant, from 20 pairs were tested in their own and in each others' unheated serum. It was found that phagocytosis was effective and that there was no difference in activity in homologous or heterologous serum. When the test was performed after the sera had been heated at 56°C. for 30 minutes, however, phagocytosis was greatly reduced. The effect of heat on the infant serum was greater than on the maternal serum.

From their results the authors concluded that cord blood is relatively deficient, compared with maternal blood, in a heat stable factor enhancing phagocytosis.

[The authors presume that there is no specific antibody to yeast cells in maternal blood; such a substance, they point out, would be heat stable. It may also be remarked that in discussing their results they assume that the loss of opsonic effect produced in sera by heating is due entirely to the loss of complement.]

*Douglas D. Smith*

HOWARD, J. G. & WARDLAW, A. C. **The Opsonic Effect of Normal Serum on the Uptake of Bacteria by the Reticulo-Endothelial System. Perfusion Studies with Isolated Rat Liver.** *Immunology.* Oxford. 1958, Oct., v. 1, No. 4, 338–52, 4 figs. [22 refs.]

The phagocytosis of bacteria by Kupffer cells has been studied by perfusing isolated rat liver with bacterial suspensions. In animals anaesthetized with nembutal, access to the portal vein was facilitated by ligaturing and cutting the oesophagus; the afferent canula was inserted into the portal vein and the efferent into the inferior vena cava through the right auricle. The heart was excised and the inferior vena cava was ligatured at a point above the renal veins. An apparatus was designed which allowed the liver to be perfused successively and at constant pressure with several different fluids containing bacteria, without stopping the flow when changing from one fluid to another. The percentage uptake of bacteria by the liver was found by making a viable count of the organisms in each fluid before and after perfusion.

When *Escherichia coli*, suspended in Ringer Locke solution containing 10% human serum, was perfused the uptake of bacteria was considerable. Suggestive that the disappearance of bacteria from the perfusate was not due to mechanical filtration was the fact that a capsulated organism, *Klebsiella pneumoniae*, resistant to phagocytosis, was less readily taken up by the liver. In addition, by histological examination of liver which had been perfused with *E. coli*, most of the organisms were found associated with the phagocytes.

The opsonic effect of normal human rat and mouse sera was demonstrated. The percentage uptake of *E. coli* suspended in these sera was much greater than when suspended in Ringer Locke only. In human serum opsonic activity was reduced by heat at 56°C. for 30 minutes, absorption with the homologous strain, or with an antibody-antigen system. The activity was completely abolished by homologous antibody absorption followed by heat at 56°C., absorption by an antibody system, or absorption by zymosan. It is concluded that the serum factors contributing to opsonic activity in this system are specific antibody, complement, and another heat labile factor. Complement alone did not act as an opsonin; the authors did not find satisfactory evidence that properdin added to complement increased significantly the uptake of bacteria.

*Douglas D. Smith*

RAFFEL, S. & NEWEL, J. M. **The "Delayed Hypersensitivity" induced by Antigen-Antibody Complexes.** *J. Exper. Med.* 1958, Dec. 1, v. 108, No. 6, 823–41, 5 figs. [25 refs.]

Experiments are described which show that the delayed hypersensitivity in guineapig skin after the injection of antigen-antibody complex in the region of antibody excess [UHR, SALVIN and PAPPENHEIMER, this *Bulletin*, 1957, v. 32, 492] can also be stimulated by injection of antigen alone. The antigen-antibody system used consisted of crystallized egg albumen and antibody produced against it in rabbits; the complex suspended in a mixture of saline, aquaphor, and paraffin oil was injected into animals either intradermally or subcutaneously. Skin tests, which consisted of the injection of egg albumen alone, revealed a reaction which could be elicited 5 days after sensitization; the reaction consisted of flat erythematous indurated lesions which remained constant in size between 24 and 48 hours after testing. The serum of these animals did not show even traces of circulating antibody. Other animals, skin tested 19 days after sensitization, gave no reaction, nor did their sera contain antibodies. The type of reaction described, although similar to the tuberculin reaction, differs from it in appearing earlier and being of shorter duration. It can be differentiated from the Arthus reaction which is more oedematous, regresses more rapidly and is associated with circulating antibodies.

Antigen alone, in doses of between 3 and 60 μgm., also gave rise to the same type of delayed hypersensitivity at 5 days, but animals sensitized in this way gave an Arthus reaction when tested at 19 days. Smaller doses of the antigen alone, 1 μgm., showed the monophasic response only, that is, a delayed hypersensitivity reaction at 5 days but no response from animals tested 19 days after sensitization.

The authors suggest that this type of delayed hypersensitivity may be related to the "tissue immunity" of tumour transplants which has been observed in mice.

*Douglas D. Smith*

SALVIN, S. B. & SMITH, R. F., with the technical assistance of Jane NISHIO. **Delayed Hypersensitivity in the Development of Circulating Antibody. The Effect of X-Irradiation.** *J. Exper. Med.* 1959, Apr. 1, v. 109, No. 4, 325–38, 4 figs. [14 refs.]

"The induction of delayed type of hypersensitivity to diphtheria toxoid in the guinea pig was not inhibited by total body irradiation up to 300 r in intensity. X-ray doses of 200 to 300 r administered about 18 hours before sensitization caused the period of delayed hypersensitivity to be extended to the 19th to 21st day postsensitization in the absence of circulating antibody. X-ray doses of 50 to 100 r caused a decrease in the titer of circulating antibody, although delayed hypersensitivity lasted for a normal time. When 300 r irradiation was administered 18 hours after sensitization, delayed hypersensitivity lasted for the usual period and circulating antibody first appeared at the usual 13 to 14 days after sensitization. Introduction of normal serum or leucocytes into irradiated animals apparently did not reduce damage to the mechanism regulating the rate of antibody synthesis."

SOBEY, W. R., ADAMS, K. M. & SHORT, B. F. **Studies in Anaphylaxis. IV. The Effects of Adjuvants and of *Haemophilus pertussis* on the Antigenic Properties of Bovine Plasma Albumin in the Mouse.** *Australian J. Biol. Sci.* 1958, Aug., v. 2, No. 3, 442–56, 6 figs. [15 refs.]

Using anaphylactic shock in mice as an indicator system, the authors have studied the relationship between shocking and sensitizing doses where the sensitizing antigen was alum precipitated. They have also compared the adjuvant effect of *Haemophilus pertussis*, a modified Freund's adjuvant and alum when used separately and mixed together. Finally a study was made of the effect of pertussis organisms in both passive and active anaphylaxis.

In these studies a shocking dose of 0·05 mgm. of bovine plasma albumin was found to be optimal for a wide range of alum-precipitated sensitizing doses which suggests that the size of the shocking dose is the important factor and not an optimal antigen-antibody ratio. The 3 adjuvants had similar capacities for enhancing anaphylactic shock whether used singly or combined. Injection of pertussis organisms 4 days before shocking in passive anaphylaxis markedly increased the anaphylactic potential. A similar increase in potential was observed in active anaphylaxis where pertussis organisms and antigen were injected at different sites 14 days before shocking. These findings suggest that pertussis organisms may enhance anaphylactic potential by some mechanism in addition to that expected from the enhancing of antibody response. *F. T. Perkins*

HALPERN, B. N., LIACOPOULOS, P., LIACOPOULOS-BRIOT, M., VAN NEER, F. & BINAGHI, R. Sensibilisation passive des tissus par des anticorps anaphylactiques *in vitro*. [**Passive Sensitization of the Tissues by Anaphylactic Antibodies** *in vitro*] *C.R. Soc. Biol.* 1959, v. 153, No. 1, 7–13, 4 figs.

HUGUES, J., BETZ, H., LECOMTE, J. & JOIRIS, E. Étude histologique des lésions initiales du phénomène de Shwartzman. [**Histological Study of the Initial Lesions of the Shwartzman Phenomenon**] *C.R. Soc. Biol.* 1959, v. 153, No. 1, 187–9.

CARACÒ, A. Sull'importanza delle plasmacellule nella produzione di anticorpi. [**Importance of Plasma Cells in the Production of Antibodies**] *Riv. Istituto Sieroterap. Ital.* 1959, Jan.–Feb., v. 34, No. 1, 22–8, 3 coloured figs. on pl. [12 refs.]

The English summary appended to the paper is as follows:—

" The behaviour of plasma cells in relation to the serum agglutinin titre has been investigated on rabbits immunized by *Salmonella typhosa*.

" A clear relationship between the number of plasma cells and the serum agglutinin titre has been found. The normal pattern of lymphatic tissues was substituted almost entirely by plasma cells proliferation.

" These findings agree with the opinion that the antibodies formation is related to the plasma cells development."

WARD, P. A., JOHNSON, A. G. & ABELL, M. R. **Studies on the Adjuvant Action of Bacterial Endotoxins on Antibody Formation. III. Histologic Response of the Rabbit Spleen to a Single Injection of a Purified Protein Antigen.** *J. Exper. Med.* 1959, May 1, v. 109, No. 5, 463–74, 10 figs. on 5 pls. [18 refs.]

STAUCH, J. E. & JOHNSON, A. G. **The Alteration of Bacterial Endotoxins by Human and Rabbit Serum.** *J. Immunology.* 1959, Mar., v. 82, No. 3, 252–63, 6 figs. [31 refs.]

With a hyperimmune rabbit serum prepared from acetone-treated cultures of *Salmonella typhi* O-901 and a purified, protein-free, lipopolysaccharide made from the same strain it was found that normal human or normal rabbit serum had the ability of altering the precipitating activity of the antigen. When, for instance, human sera from healthy donors were incubated with this purified polysaccharide (endotoxin) for various periods at 37°C., its precipitating ability, as compared with the controls, was reduced by 40–70%. This inactivating power of normal sera depended on a number of factors. At temperatures 0–4°C. there was no loss but as the temperature rose and as the time of incubation of the mixture of serum and endotoxin increased, provided the *p*H was in the region of 7·0, the precipitating power decreased and was completely lost after incubation at 65°C. for 6 hours. The properdin system was excluded as influencing the reaction and lysozyme was found to have no effect. It is suggested that the alteration may be due to enzymatic degradation of the endotoxin. *H. J. Bensted*

SORKIN, E. & BOYDEN, S. V. **Studies on the Fate of Antigens** *in vitro*. **I. The Effect of Specific Antibody on the Fate of $I^{131}$-Trace Labeled Human Serum Albumin** *in vitro* **in the Presence of Guinea Pig Monocytes.** *J. Immunology.* 1959, Apr., v. 82, No. 4, 332–9, 4 figs. [30 refs.]

WHITEHOUSE, F., Jr. & ULRICH, Gwen. **Enzymatic Digestion of Rabbit Globulin.** *Proc. Soc. Exper. Biol. & Med.* 1959, Apr., v. 100, No. 4, 792–6, 2 figs. [10 refs.]

HEMMINGS, W. A. & MORRIS, I. G. **An Attempt to affect the Selective Absorption of Antibodies from the Gut in Young Mice.** *Proc. Roy. Soc.* Ser. B. 1959, Apr. 21, v. 150, No. 940, 403–9. [11 refs.]

" In young mice, antibodies from immune sera in the gut pass readily into the circulation. This process is selective in that the amount of antibody reaching the circulation depends on the species of origin of the immune serum. The relative ease of entry of some antibodies are rabbit 1, guinea-pig 2·4, and mouse 4·5. The ability to absorb antibodies from the gut decreases sharply at 15 to 17 days, although the amount of homologous iodinated γ-globulin absorbed at 20 days is quite appreciable. Ingestion of the ε-toxin of *Clostridium welchii* was without demonstrable effect on the selective absorption of antibodies from the gut of young mice."

LUZZIO, A. J. **Effects of X-Rays on Hemagglutinins.** *J. Infect. Dis.* 1959, Mar.–Apr., v. 104, No. 2, 152–5. [15 refs.]

" Exposure of human red blood cell agglutinins in immune serums to X rays resulted in the inactivation of specific groups. Other blood group determining sites remained unaffected at the same dose levels. The results indicate that various antibody-combining sites possess specific radiosensitivities. The practical applications of ionizing radiations as a tool in studying antibody-combining site structure are discussed."

KOSCHUCHAROFF, P. Ein Beitrag zur Gewinnung von hochwertigem hämolytischem Ambozeptor. [**The Preparation of Highly Potent Haemolytic Antibodies (Amboceptor)**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 7/8, 609–13, 1 fig. [12 refs.]

One of the greatest difficulties in obtaining high titre amboceptor is the rapidly increased sensitivity of the rabbits to the red blood cells. The authors used various methods including injection of ganglion blocking reagents and antihistamine preparations to suppress anaphylactic shock without interference with production of haemolysin. They found that anaphylactic shock can be suppressed by intravenous injection of antihistamine preparations shortly before injection of the red cells and thus a high titre serum obtained with very few deaths. *P. A. Clearkin*

GOODMAN, H. S. **Immune Hemolysis: Determination of Values for Optimal and Maximal Sensitization. Comparison in Several Hemolytic Systems.** *Proc. Soc. Exper. Biol. & Med.* 1959, Apr., v. 100, No. 4, 789–92, 3 figs.

SEWELL, M. M. H. **Normal Components of Guinea Pig Serum which may cause Antigens to show an Apparent Anti-Complementary Effect.** [Correspondence.] *Nature.* 1959, Apr. 11, v. 183, 1062.

Experiments suggest that complementary activity of guineapig serum may be diminished, in complement-fixation tests, by the formation of a properdin-antigen complex which inactivates C′3. Complement titres fell markedly in the presence of a "zymosan-properdin" complex and also in the presence of Wassermann antigen. [Whether the same mechanism was responsible for the loss of complement in both cases was not shown.] *J. G. P. Hutchison*

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# Miscellaneous

QUEENSLAND INST. OF MED. RES. **Thirteenth Annual Report of the Council of the Queensland Institute of Medical Research to the Honourable the Minister for Health and Home Affairs; Year ended 30th June, 1958.** 21 pp. 1958. Brisbane: A. H. Tucker, Govt. Printer.

In this the 13th Annual Report of the Council of the Queensland Institute of Medical Research, the Director presents an interesting account of the many subjects on which scientific work was done. There is also a considerable list of papers published during the year 1957–8.

Under the heading of bacteriology there are accounts of studies of intestinal allergy in guineapigs, and of epidemiological investigation of 3 institutional epidemics due to salmonella infection in 1 instance, to *Shigella sonnei* and *Escherichia coli* 055 in a home for mothers and children and to *Pseudomonas pyocyanea* in an ophthalmic ward. Other studies included the investigation of maternal antibodies against coliform organisms.

*Toxoplasma* investigations comprised an extension of the survey of the normal population for antibodies, not adequately covered in last year's report. Surveys of the sera of many different kinds of animals for their complement-fixation titres were also carried out. Experiments were made on the isolation of *Toxoplasma* from animals by mouse inoculation.

In virology many studies are reported. These include studies of arthropod-borne viruses, survey of blood from aborigines for neutralizing antibodies to Murray Valley encephalitis virus, similar surveys of animal sera, virus infections in animals, influenza investigations in man and the control of psittacosis.

At the Innisfail Field Station the survey of infections in animals particularly in respect of their possible transmission to man was greatly expanded.

There are also short reports on hookworm investigations, filariasis, tapeworm in man, the parasites of native animals and on entomological studies.

[For an abstract of the Twelfth Report, see this *Bulletin*, 1958, v. 33, 471.] *M. E. Delafield*

CHINESE MED. J. Peking. 1959, Feb., v. 78, No. 2, 103–5. **Recent Achievements in the Promotion of Traditional Chinese Medicine.**

Following a Party directive in 1955 some 300 doctors trained in western medicine received instruction in traditional Chinese medicine in 6 cities by means of courses lasting 2½ years, and they are now practising both forms of medicine. Short and sparetime courses have also been organized at which several thousand doctors have been given elementary instruction in traditional methods. A popular campaign has collected valuable tested and secret traditional remedies which are being preserved by sending qualified doctors to study under traditional "doctors" who are also training some 70,000 apprentices. 13 colleges, hundreds of schools and over 300 hospitals of traditional medicine have been established; traditional medical classics are being translated into modern language and text books are being compiled. Wild medicinal herbs are being cultivated and animals collected. Astonishing successes are claimed for treatment by traditional methods and it is stated that the broad masses of the people welcome this revival. *T. H. Davey*

CHINESE MED. J. Peking. 1959, Feb., v. 78, No. 2, 106–10. **Acupuncture and Moxibustion in Treatment of Bacillary Dysentery. Clinical Observations on 63 Cases.**

Doctors trained in both western and traditional Chinese medical methods compared the results of treatment of bacillary dysentery by western drugs and by acupuncture and moxibustion (*i.e.* counter-irritant treatment by the insertion of needles and by the application of heat at particular anatomical sites which vary with the symptom being treated). Acupuncture and moxibustion were used in 28 cases, sulphaguanidine in 30, herbal remedies in 9 and bacteriophage in 12. The first treatment gave the quickest relief of symptoms and return of stools to normality. In a second series of 35 cases of Sonne and Flexner dysentery (19 of them yielding positive stool cultures), and 3 carriers (2 Sonne and 1 Flexner) the traditional treatment was similarly effective. Negative stool cultures were the criterion of cure [but only 19 of 35 gave positive cultures] and in the 3 carriers 10 consecutive negative cultures were obtained. Both acupuncture and moxibustion were performed once daily on all acute cases except those with high fever, and moxibustion was the main treatment of carriers. Details of the clinical condition and treatment of 4 patients by traditional methods are given. The anatomical points for acupuncture and moxibustion in a variety of diseases are given by letter references but only 6 of them in English in sufficient detail to identify the point. *T. H. Davey*

GREENWALD, I. **Goitre in Japan.** *Trop. & Geograph. Med.* Amsterdam. 1958, June, v. 10, No. 2, 149–53. [Numerous refs.]

" One of the great supports for the hypothesis that endemic goitre is due to lack of iodine is its supposed rarity in Japan." A map published by the Iodine Educational Bureau in 1946 indicated that Japan was free from goitre, nevertheless the review of the literature presented in this paper shows that this is by no means true. The first report on endemic goitre in Japan appears to be one published in 1899. Since that time a considerable number of reports have shown that endemic goitre exists in all the 4 principal islands of Japan. In the earlier accounts the reported incidence of simple goitre appeared to be low but that of hyperthyroidism to be high which may have been due to the fact that little official attention was given to non-toxic goitres. Later observations were to the effect that in some localities the incidence of simple goitre was high. From studies carried out in Hokkaido the interesting observation was made that goitre was common in the coastal areas but much less frequent in the interior.

Much of the literature here reviewed is Japanese, very little of which has been available to the Western world. In the summary of this review it is stated: " It is difficult to reconcile the iodine-lack hypothesis with these findings." *M. E. Delafield*

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# Book Review

VIJIL, C. [Ph.B., M.D., M.Sc., M.P.H.]. **Public Health and Social Science.** 78 pp. 1959. Copenhagen: Ejnar Munksgaard, 6, Nörregade. [Kr. 12.50.]

This small book consists of a preface in which the author states that it is intended for students " to awake their interest to the need to use social science in their daily practical activities ", and 6 short chapters dealing with ethnology, sociology and social psychology in relation to public health, and with some basic facts about human and animal populations. Each chapter contains a bibliography which should be useful to students; almost all the references are to publications in the English language.

There is a lot of good sense in the author's insistence that disease is more complex than we used to think, and that one single element such as an infection, or even a group of elements such as economic and social inequalities, may be only part of the story; he insists that " cultural phenomena are to be considered as the deep roots of illness ". He goes on to discuss the sociology of disease and the complex interactions of the individual, the family group and the large community, all powerfully swayed by beliefs which may have originated in magical or religious conceptions of disease, and the obvious but neglected fact that it is necessary to take these into account. This of course is particularly important in many tropical communities which have not yet shaken free from the view that disease is a punishment or is deliberately engineered by an enemy, and which tend to ask " who has caused it? " rather than " what has caused it? ". But equally the author stresses the fact that in the more scientifically developed communities the social and cultural pressures, though different, are still formidable in their bearing on health. He ends a valuable collection of notes as follows:—

" A science of men is being created. In Public Health we must grow out of the age of the microscope, temperate enthusiasms for sera vaccines, miracle drugs and insecticides, be wary of kits and fool proof techniques and turn our attention to the people. Use of these niceties will be more effective.

" The problems with which we have still to grapple are very serious everywhere. Well conducted research towards elucidating their cultural social, individual and collective social psychological elements will prevent a good deal of suffering distress and misery."

*Charles Wilcocks*

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